What operational activities are required as part of non-clinical research?

What licenses and/or approvals are required to conduct research?

What key regulatory steps are required to receive marketing authorisation?

What advice is available for non-clinical research development?

What programmes are available to accelerate time to market?

What follow-up activities are required after patient treatment?

What steps are required for clinical trial application?

What clinical trial steps should be performed prior to marketing authorisation?

What key steps are required to provide ATMPs to patients?

What programmes are available to accelerate time to market?

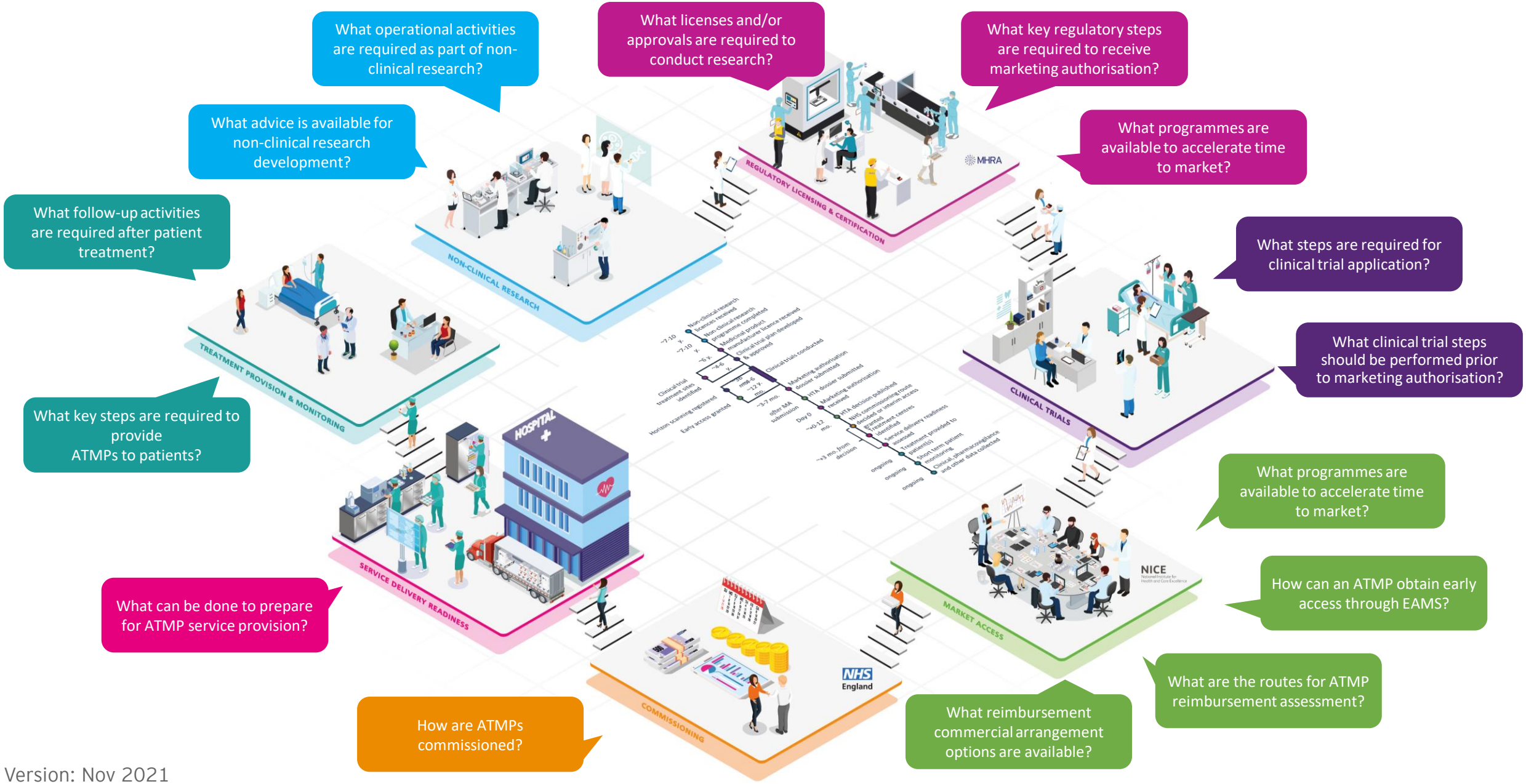
How can an ATMP obtain early access through EAMS?

What can be done to prepare for ATMP service provision?

What are the routes for ATMP reimbursement assessment?

What reimbursement commercial arrangement options are available?

How are ATMPs commissioned?




Version: Nov 2021

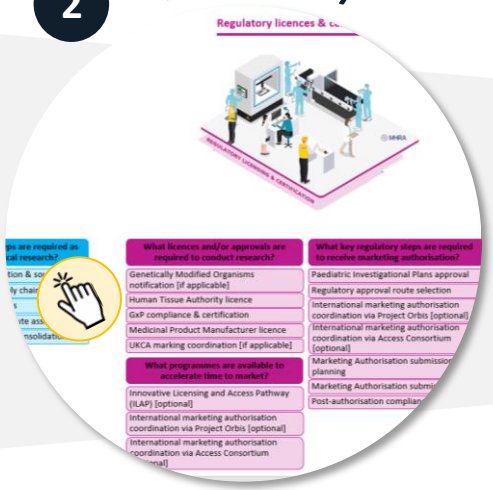
# How to use the Roadmap Tool

## 1 Roadmap overview


Explore the ATMP Roadmap overview to view all the sections and guiding questions included in the Tool.

**Click the section of the Roadmap you would like to find out more about.**
*You will be taken to the first Topic deep-dive slide of that section.*

## 2 Topic summary




Explore the Topic summary to view all the individual topics that are covered throughout the Tool.

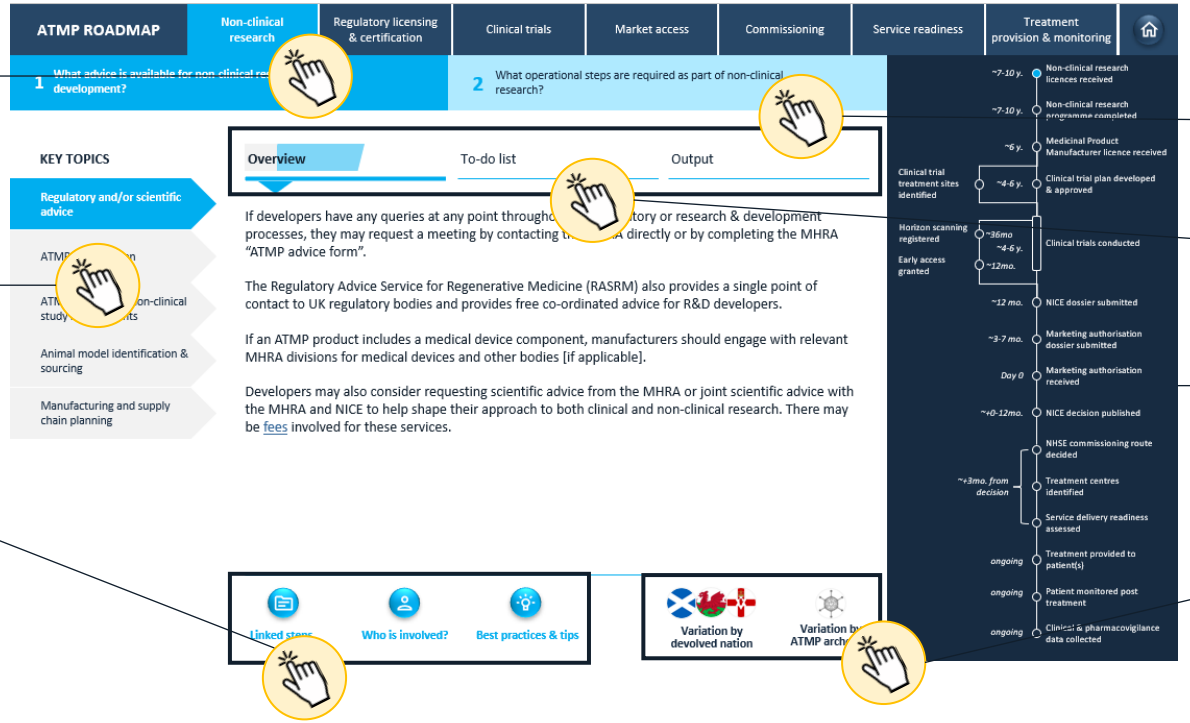
**Click to the question or topic you would like to find out more about.**
*You will be taken to the Topic deep-dive slide.*

## 3 Topic deep-dives

Navigate by Roadmap section

Navigate by topic

Click to view “Linked steps”, “Who is involved” and “Best practices & tips”




Navigate by question

Click to view information on “Overview”, “To-do list” and “Output” tabs

Track progress along the ATMP pathway through the timeline

For topics where variance by devolved nation exists, click the flag to view nation-specific slides. For topics where variance by ATMP archetype exists, the icon will appear

## What is the ATMP Roadmap Tool?

This Roadmap Tool sets out the key steps and activities in the end-to-end pathway for Advanced Therapy Medicinal Products (ATMPs) in England from non-clinical research through to patient treatment. The pathway signposts where differences exist between devolved nation (Scotland, Wales and Northern Ireland) and ATMP archetype (listed below):

- **Gene therapies** (modification of the genetic material of living cells within or outside the body – *in vivo* and *ex vivo*)
- **Somatic cell therapies** (the administration of human living cells which have been manipulated or processed outside the body – *ex vivo*)
- **Tissue-engineered products** (which contains cells or tissues administered with a view to regenerating, repairing or replacing a human tissue)

England has a nationalised healthcare system with a single payer, NHS England, a single regulator, MHRA, and a single Health Technology Assessment body, NICE, which makes market access reimbursement decisions. In order for a medicine to be commissioned as decided by the NHS in each devolved nation of the UK, the medicine must be licensed by the MHRA and undergo a Health Technology Assessment by NICE (or the applicable devolved nation body). Descriptions of these, and other interacting stakeholders that are referenced throughout the ATMP Roadmap can be found here along with a description of their role.

## Who should use this Roadmap Tool?

A significant number of ATMPs are due to be assessed for potential reimbursement in the coming years; this Roadmap Tool has primarily been designed for ATMP developers and other ecosystem partners & stakeholders looking to navigate England's ATMP landscape and gain a deeper understanding of:

- Steps and activities that are mandatory (and optional) at each stage of the ATMP pathway
- When these steps and activities should be conducted
- The external guidance available at each stage of the ATMP Roadmap and where to find it
- The stakeholders involved at each point through the pathway
- Best practices/tips to help navigate the pathway

## How was the Roadmap created?

Please see the following page for acknowledgements, information on funding and development, how the Roadmap is kept up to date and referencing of the document

## What best practice principles should Roadmap users keep in mind?

There are some suggested best practice principles to keep in mind whilst bringing ATMPs through the end to end pathway which will support in bringing these drugs to NHS patients as efficiently as possible.

**Engage early**

Early engagement and collaboration between ATMP manufacturers and healthcare system stakeholders such as MHRA, NHSE and NICE during the product development and regulatory stages of the pathway can ensure alignment on future product-specific requirements and therefore ensure system readiness.

**Seek advice and support**

Take advantage of the wide range of available guidance and support offered by NHS and other ATMP ecosystem stakeholders throughout the ATMP pathway in order to gain a understanding of the UK landscape and how to meet the specific requirements of the regulators, commissioners and providers.

**Minimise complexity**

ATMPs are by nature very complex medicines, but seek to minimise additional complexity where possible and look for where standardisation can occur across ATMPs e.g. through service delivery requirements in order to speed up time to market and patient access.

**Patient centricity**

Keep the patient in mind throughout the end-to-end pathway and engage with patient groups to keep them at the heart of development, ensuring consideration of the diversity of patient populations.

Next >

**Acknowledgements**

The content of the ATMP Roadmap was provided by multiple contributors including members of The Accelerated Access Collaborative (AAC) ATMP Workstream 3: The Association of the British Pharmaceutical Industry (ABPI), Cell and Gene Therapy Catapult, The Medicines and Healthcare products Regulatory Agency (MHRA), The Midlands and Wales Advanced Therapy Treatment Centre (MW-ATTC), NHS England (NHSE), The National Institute for Health and Care Excellence (NICE), The NHS Specialist Pharmacy Service (SPS)

**Funding and development**

The development of the ATMP Roadmap was funded by The Association of the British Pharmaceutical Industry (ABPI) and the following pharmaceutical companies: Amicus Therapeutics UK Ltd, Bayer Plc, bluebird bio UK Ltd, Janssen-Cilag Ltd, Novartis Pharmaceuticals UK Ltd and Pfizer Ltd. The ATMP Roadmap was created by Ernst & Young (EY). Please email any comments or feedback to ATMP@ABPI.org.uk

**Reference**

If using the content please reference the document as follows
AAC and ABPI, 2021. The AAC and ABPI ATMP Roadmap. [Online] Available at: www.abpi.org.uk/publications/advanced-therapy-medicinal-products-atmps-roadmap-tool

**< Previous**

## Non-clinical research


| What advice is available for non-clinical research development? |
|---|
| Regulatory and/or scientific advice |
| ATMP classification |
| ATMP quality and non-clinical study requirements |
| Animal model identification & sourcing |
| Manufacturing and supply chain planning |

| What operational steps are required as part of non-clinical research? |
|---|
| Animal model identification & sourcing |
| Manufacturing and supply chain planning |
| *In vitro and in vivo* studies |
| Delivery and diagnostic route assessment |
| Research documentation consolidation |

## Regulatory licences & certification


| What licences and/or approvals are required to conduct research? |
|---|
| Genetically Modified Organisms notification [if applicable] |
| Human Tissue Authority licence |
| GxP compliance & certification |
| Medicinal Product Manufacturer licence(s) |
| UKCA marking coordination [if applicable] |

| What programmes are available to accelerate time to market? |
|---|
| Innovative Licensing and Access Pathway (ILAP) [optional] |
| International marketing authorisation coordination via Project Orbis [optional] |
| International marketing authorisation coordination via Access Consortium [optional] |

| What key regulatory steps are required to receive marketing authorisation? |
|---|
| Paediatric Investigational Plans approval |
| Regulatory approval route selection |
| International marketing authorisation coordination via Project Orbis [optional] |
| International marketing authorisation coordination via Access Consortium [optional] |
| Marketing Authorisation submission planning |
| Marketing Authorisation submission |
| Post-authorisation compliance |

More topics >

## Clinical trials


| What steps are required for clinical trial application? |
|---|
| GxP compliance & certification |
| Expert Advisory Group Clinical Trial Assessment [if applicable] |
| Clinical trial planning, design & protocol development |
| Governance & process documentation |
| Informed consent procedure development |
| Clinical trial registration |
| Clinical trial authorisation |
| Research documentation consolidation |
| Trial recruitment |

| What clinical trial steps should be performed prior to marketing authorisation? |
|---|
| Clinical trial reporting |
| End of trial declaration |
| Subsequent trial phase completion |
| Horizon scanning registration |

## Market access


| What programmes are available to accelerate time to market? |
|---|
| Innovative Licensing and Access Pathway (ILAP) [optional] |
| International marketing authorisation coordination via Project Orbis [optional] |
| International marketing authorisation coordination via Access Consortium [optional] |

| How can an ATMP obtain early access through EAMS? |
|---|
| Promising Innovative Medicine designation [optional] |
| EAMS scientific opinion [optional] |

| What are the routes for ATMP reimbursement assessment? |
|---|
| Early advice on Market Access process [optional] |
| Health Technology Assessment Technology Appraisal |
| Health Technology Assessment Highly Specialised Technologies evaluation |

| What reimbursement commercial arrangement options are available? |
|---|
| Patient Access Scheme [optional] |
| Commercial Access Agreement [optional] |
| Managed Access Agreement [optional] |

< Previous topics

More topics >

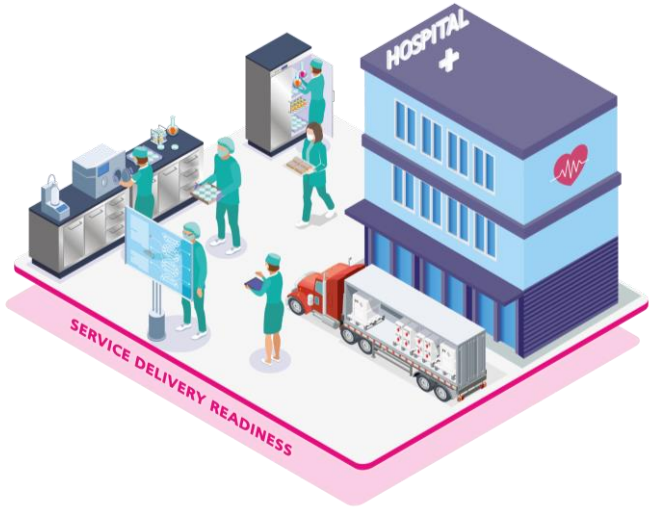
Topic summary (2/3)

## Commissioning


**How are ATMPs commissioned?**

- Routine commissioning
- Commissioning via Managed Access

## Service delivery readiness




**What can be done to prepare for ATMP service provision?**

- Service delivery readiness
- Treatment centre identification

## Treatment provision & monitoring

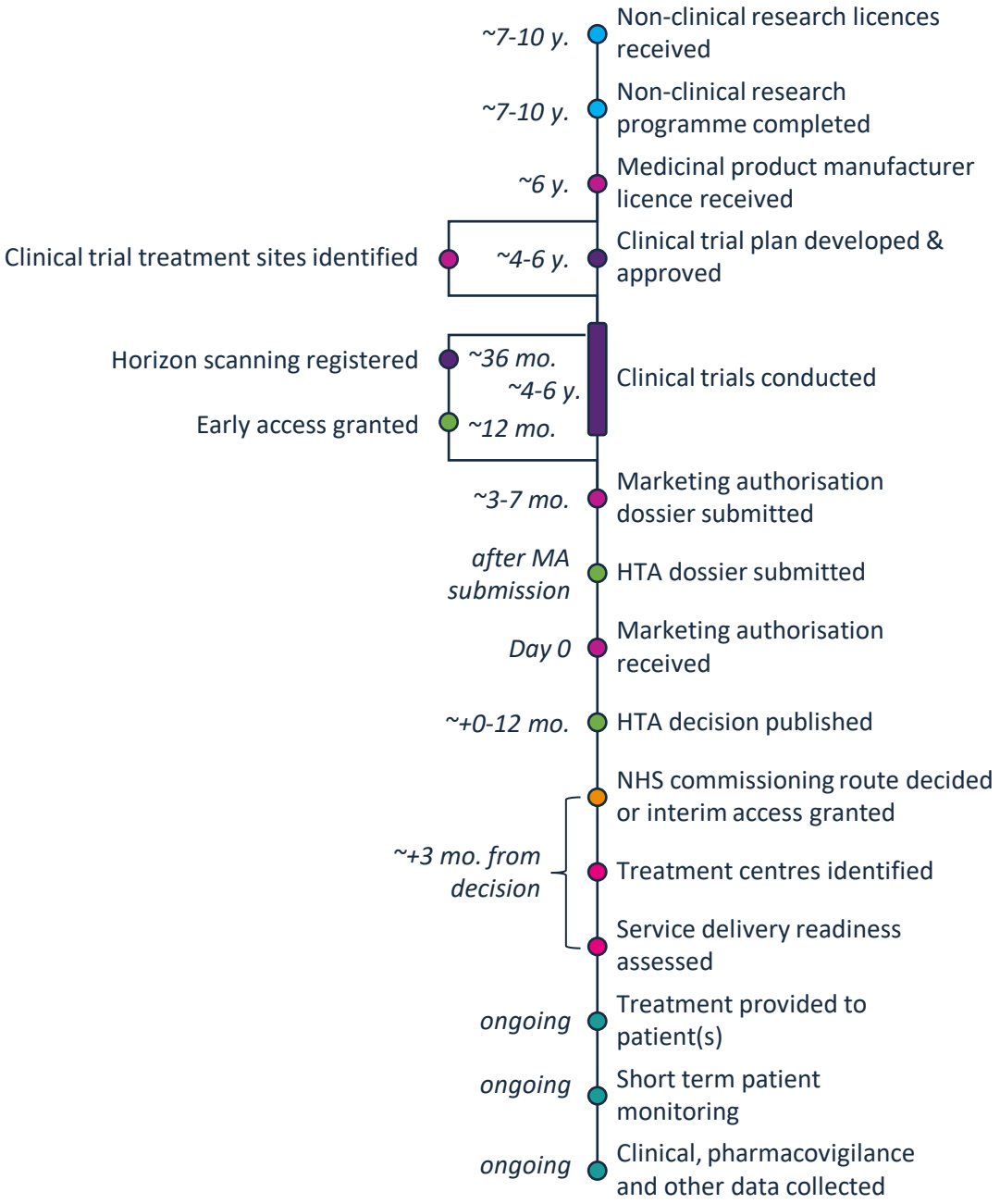

**What key steps are required to provide ATMPs to patients?**

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short term patient monitoring

**What follow-up activities are required after patient treatment?**

- Data collection

< Previous topics




**Milestone key**

- Non-clinical research
- Regulatory licences & certification
- Clinical trials
- Market access
- Commissioning
- Service delivery readiness
- Treatment provision & monitoring

**Please note that many steps and activities required to reach each milestone will occur in parallel and are not fully sequential. Refer to each section and topic for more details. All timings are estimates, will vary based on individual ATMP and are intended to be used as a guide. Timings provided are related to time of marketing authorisation (day 0). Not all milestones or commissioning routes etc. detailed in the roadmap are included in this summary timeline.*

# Timelines & milestones

**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

**Overview** | To-do list | Output

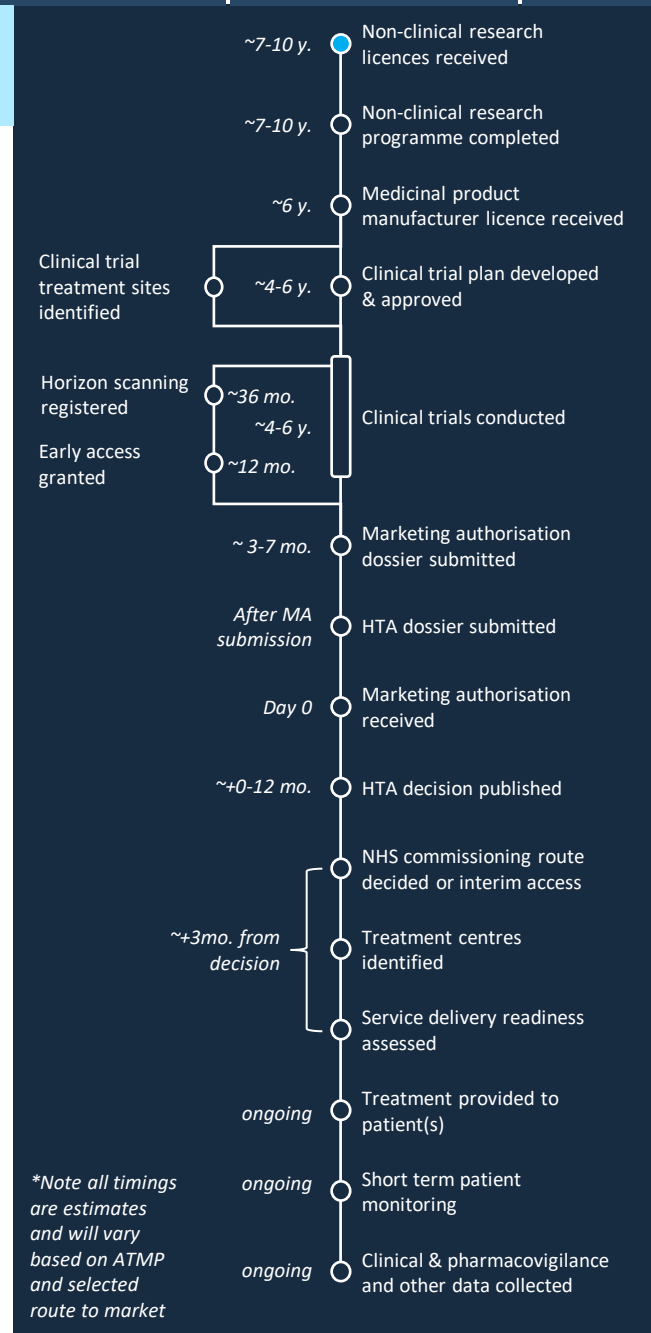
If developers have any queries at any point throughout the regulatory or research & development processes, they may request a meeting by contacting the MHRA directly or by completing the MHRA "ATMP advice form".

The Regulatory Advice Service for Regenerative Medicine (RASRM) also provides a single point of contact to UK regulatory bodies and provides free co-ordinated advice for R&D developers.

If an ATMP product includes a medical device component, manufacturers should engage with relevant MHRA divisions for medical devices and other bodies [if applicable].

Developers may also consider requesting scientific advice from the MHRA or joint scientific advice with the MHRA and NICE to help shape their approach to both clinical and non-clinical research. There may be fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

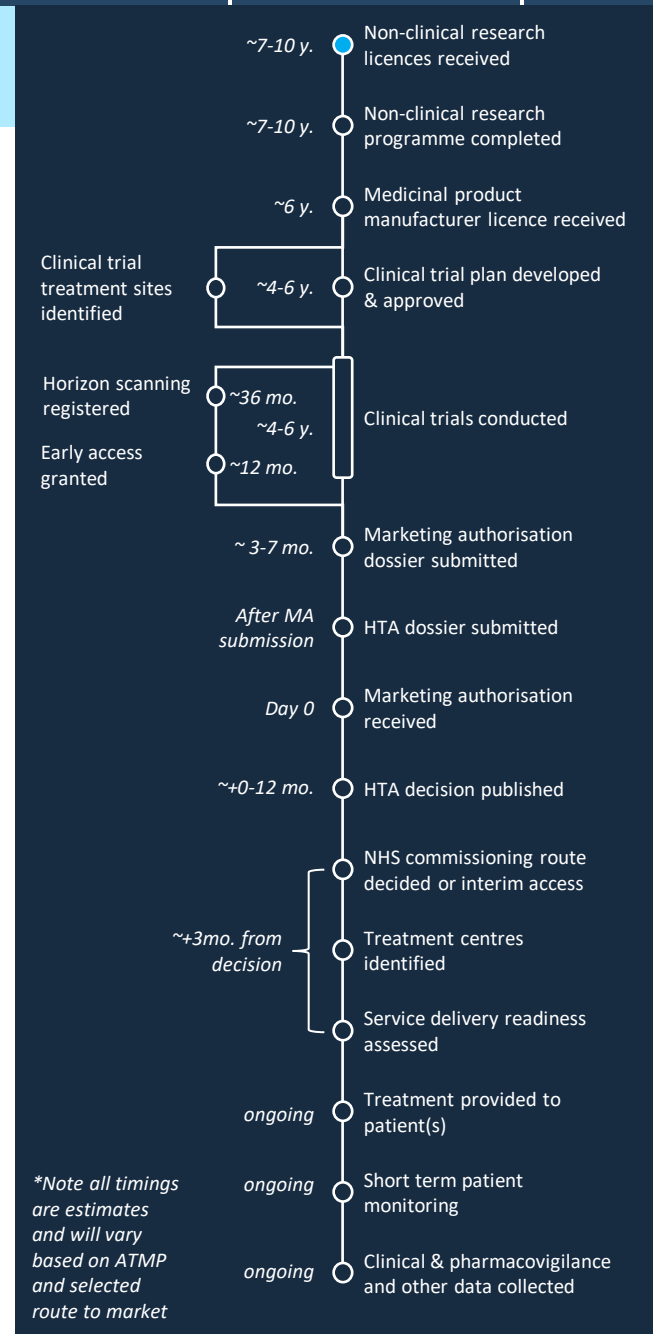
Overview | **To-do list** | Output

- Request a free meeting with the MHRA innovation office here
- Review guidance from the MHRA on regulation of ATMPs here
- Request regulatory advice from the MHRA by completing the ATMP advice form here
- Contact the Regulatory Advice Service for Regenerative Medicine (RASRM) by calling the MHRA customer services team on 0203 080 6000 or email info@mhra.gov.uk
- Consider requesting joint scientific advice with the MHRA and NICE here
- ATMP developers can also register with the NHS Innovation service here, at any point throughout the development process

**When**

At any point throughout the R&D and regulatory processes

Linked steps | Who is involved? | Best practices & tips



# 1 What advice is available for non-clinical research development?

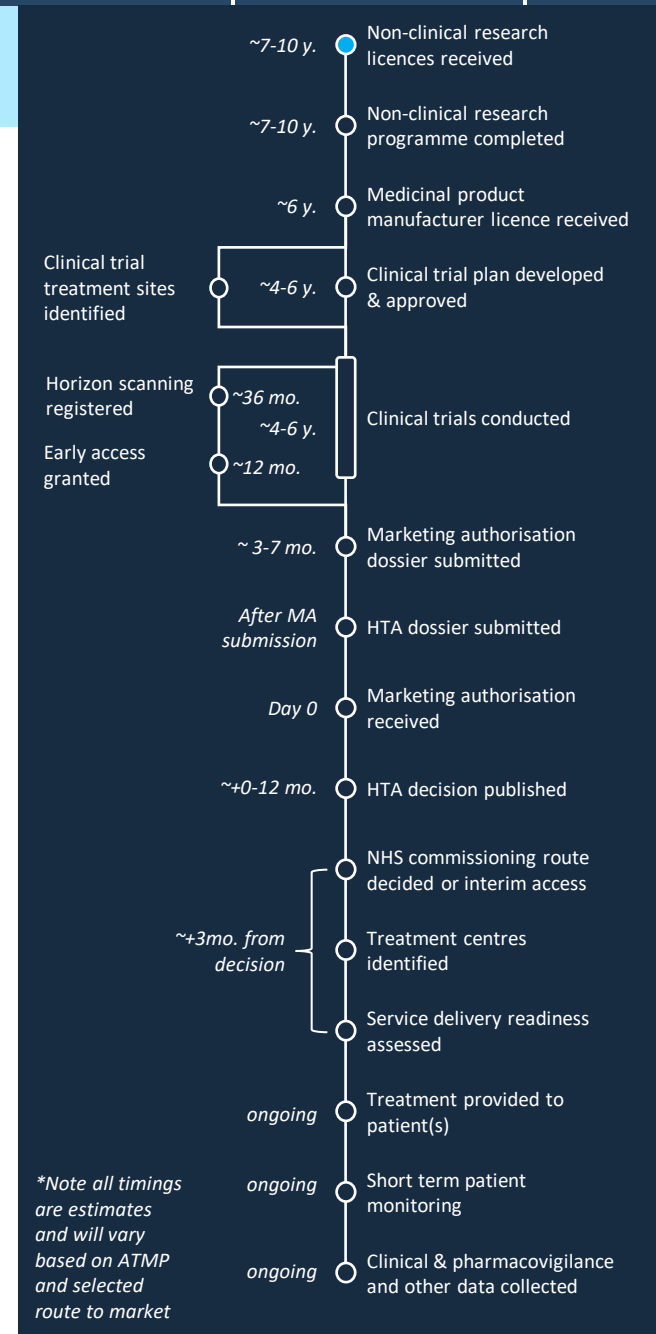
2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

Overview | To-do list | **Output**

- Tailored regulatory advice from the MHRA
- ATMP developer and MHRA meeting
- Joint scientific advice from MHRA and/or NICE




Linked steps | Who is involved? | Best practices & tips

# 1 What advice is available for non-clinical research development?

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

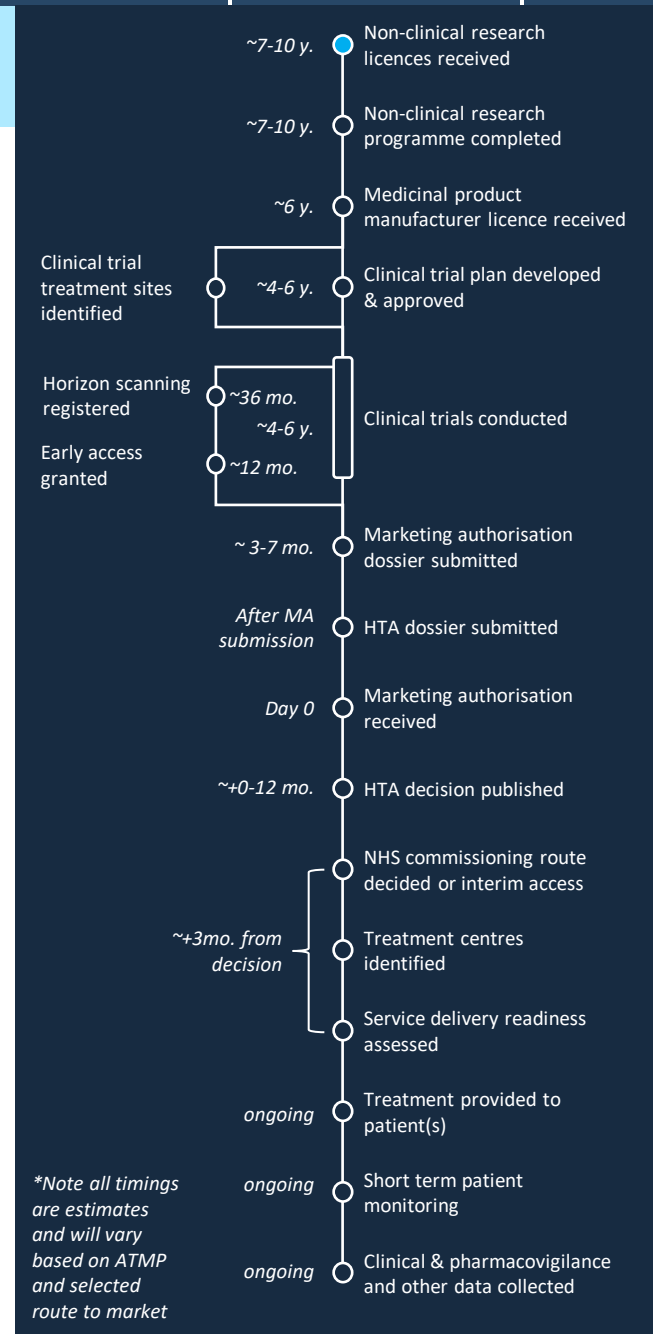
## Overview

## To-do list

## Output

**Refer to all subsequent topics**

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
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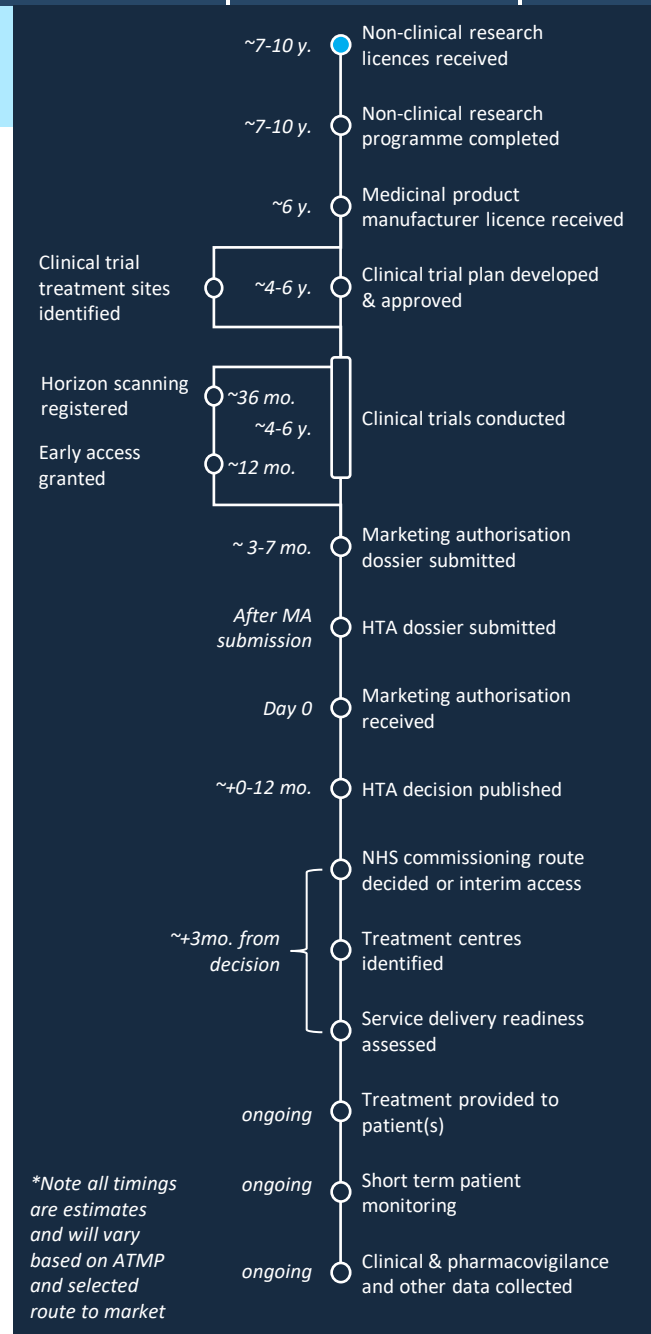
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- RASRM
- NICE

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- **Regulatory and/or scientific advice**
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

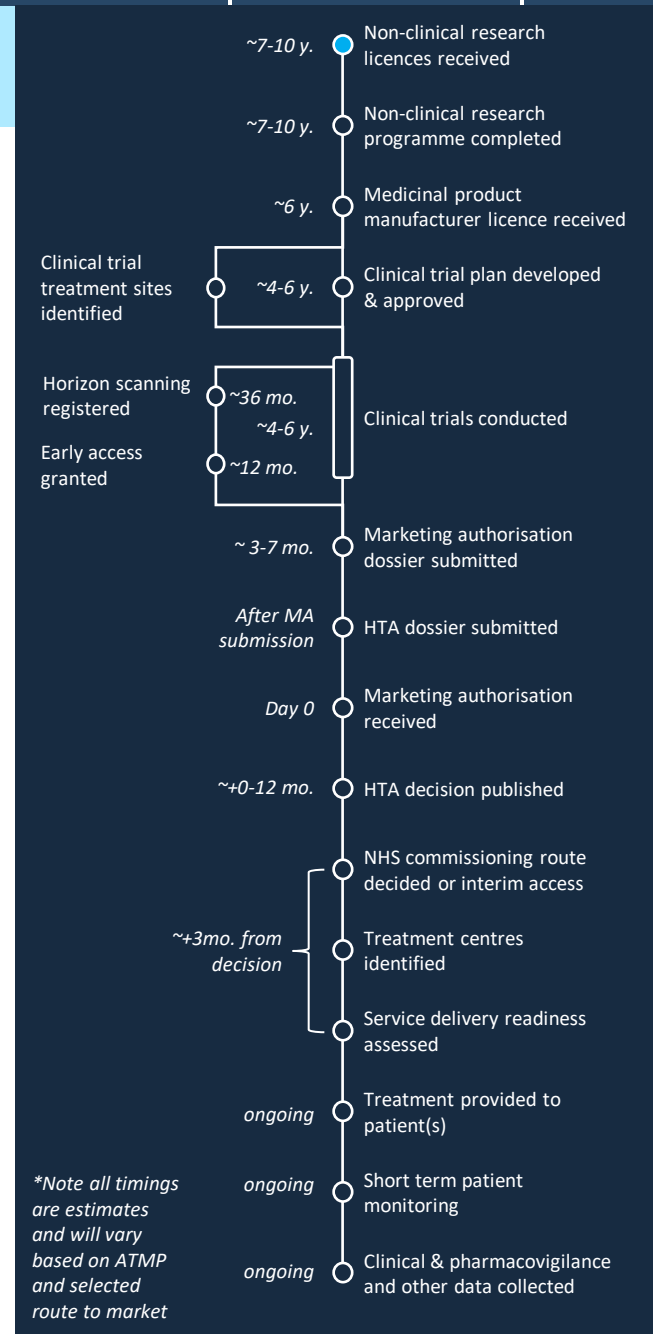
## Overview

- For ATMPs, engagement with MHRA at an early stage is recommended
- Developers should request Scientific Advice as soon as is feasible during the research & development process as it may take some time to receive a response and the Scientific Advice will help ensure they are progressing along the correct lines with their ATMP development
- Developers should also ensure to be specific in their advice inquiries

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

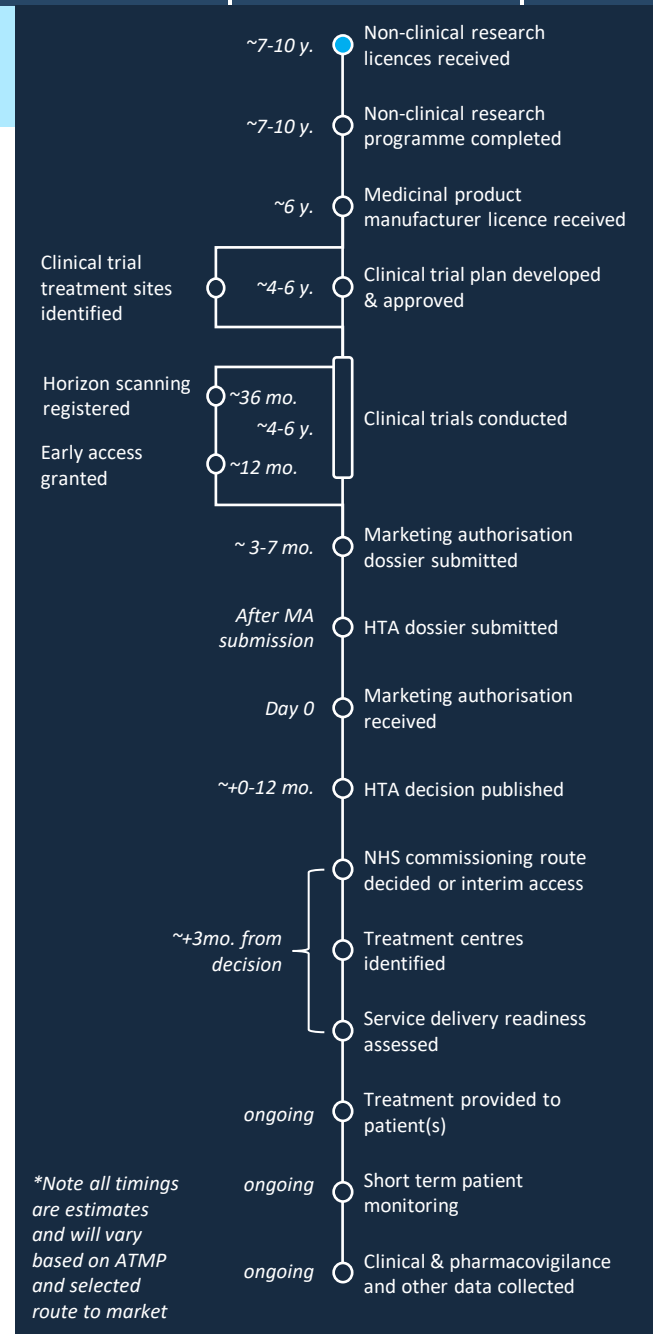
## KEY TOPICS

- Regulatory and/or scientific advice
- **ATMP classification**
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

**Overview** | To-do list | Output

Manufacturers must identify their drug's ATMP type according to MHRA classification. If there is uncertainty, fill out the MHRA ATMP advice form or consult the MHRA/EMA guidance on ATMP classification. There may be fees involved for these services.

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- **ATMP classification**
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

Overview | **To-do list** | Output

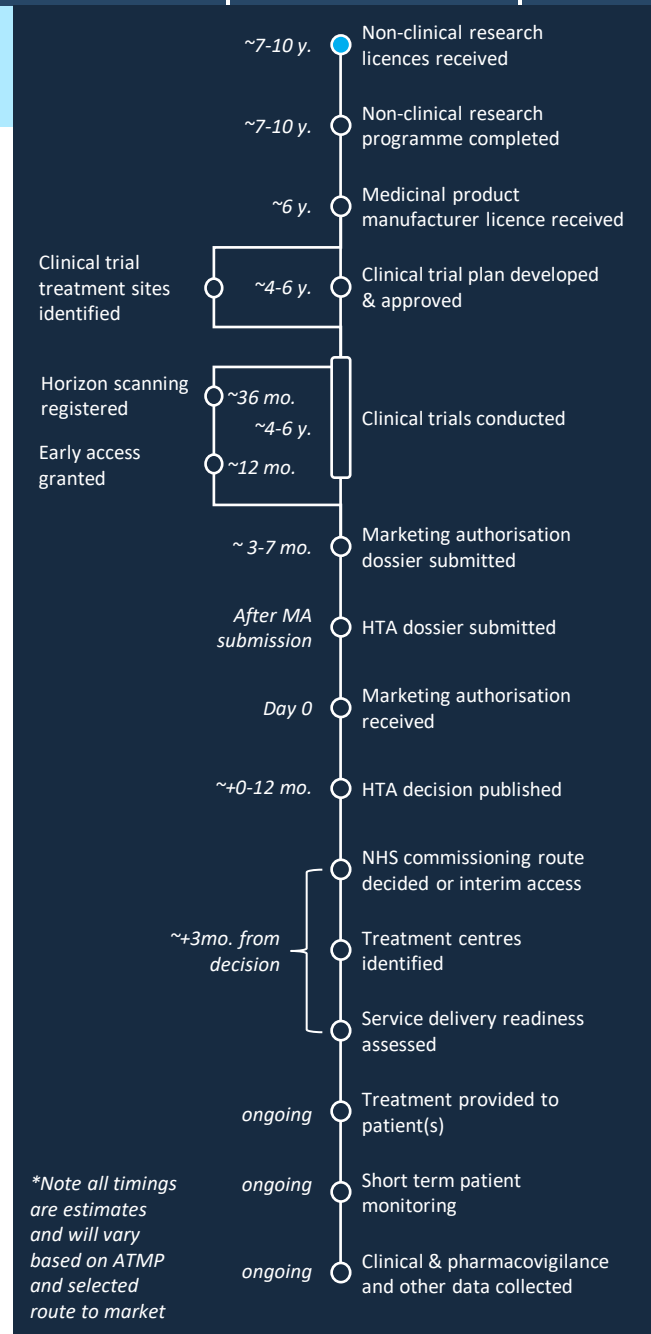
- Review guidance on ATMP classification from MHRA here
- Fill out the MHRA ATMP advice form which can be accessed here
- You can also visit the EMA guidance here for guidance on ATMP classification or apply to get an opinion from the Committee for Advanced Therapies (CAT)*

**When**

Classification can occur during or after drug discovery phase, and advice can be requested at any point throughout process but ideally prior to commencing non-clinical research

*EMA ATMP specific guidelines are still recommended as a useful source of guidance post-brexit transition

Linked steps | Who is involved? | Best practices & tips



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

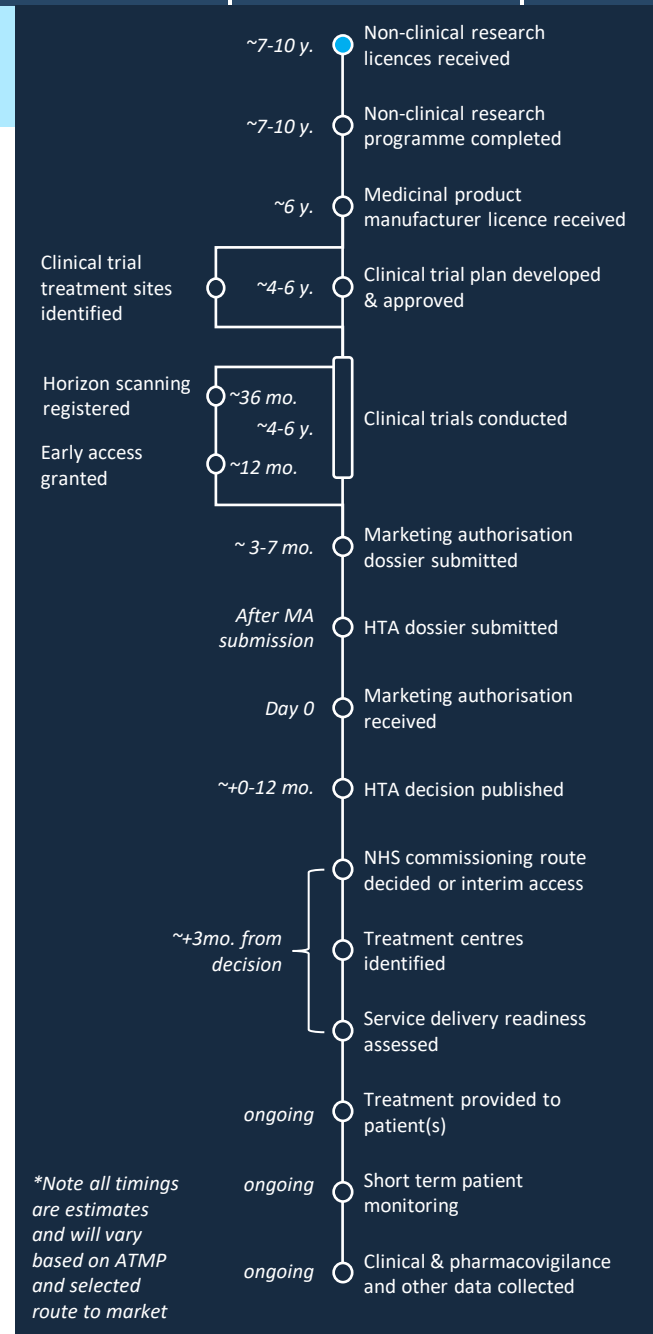
## KEY TOPICS

- Regulatory and/or scientific advice
- **ATMP classification**
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

Overview | To-do list | **Output**

- Identification of ATMP as gene therapy medicinal product, a somatic cell therapy medicinal product or a tissue engineered product
- The MHRA advice on ATMP in response to form submission

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- **ATMP classification**
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- Manufacturing and supply chain planning

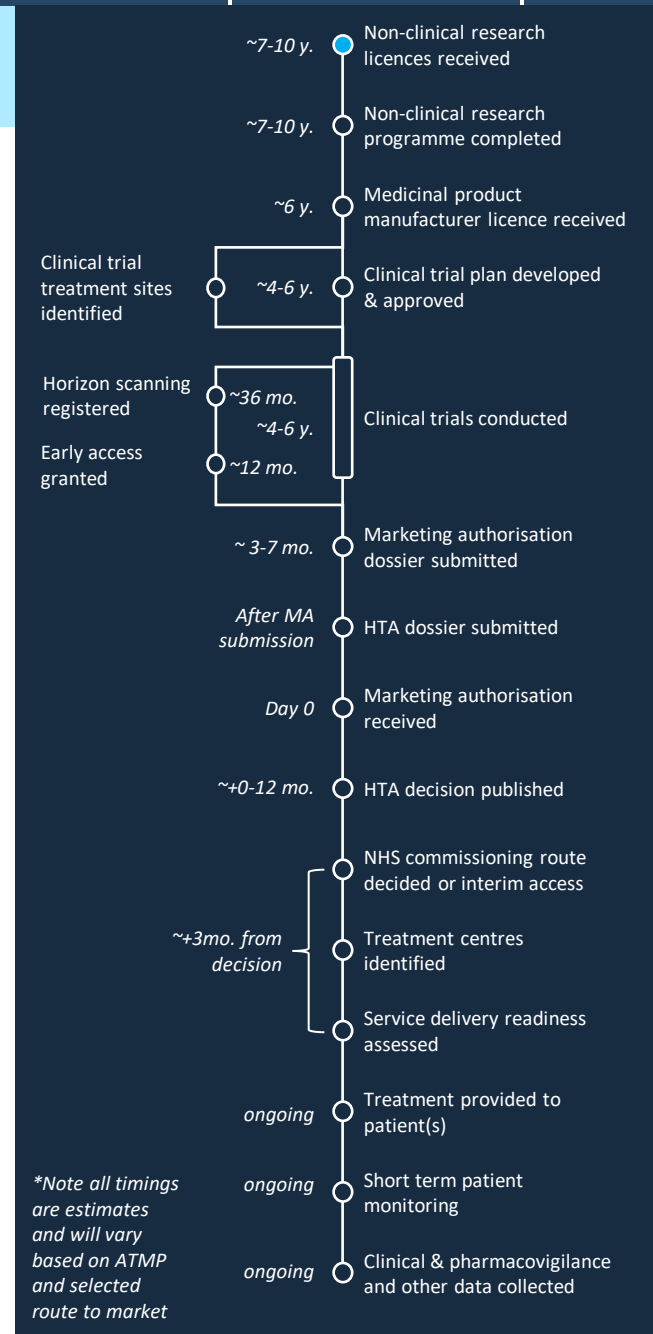
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

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## KEY TOPICS

- Regulatory and/or scientific advice
- **ATMP classification**
- ATMP quality and non-clinical study requirements
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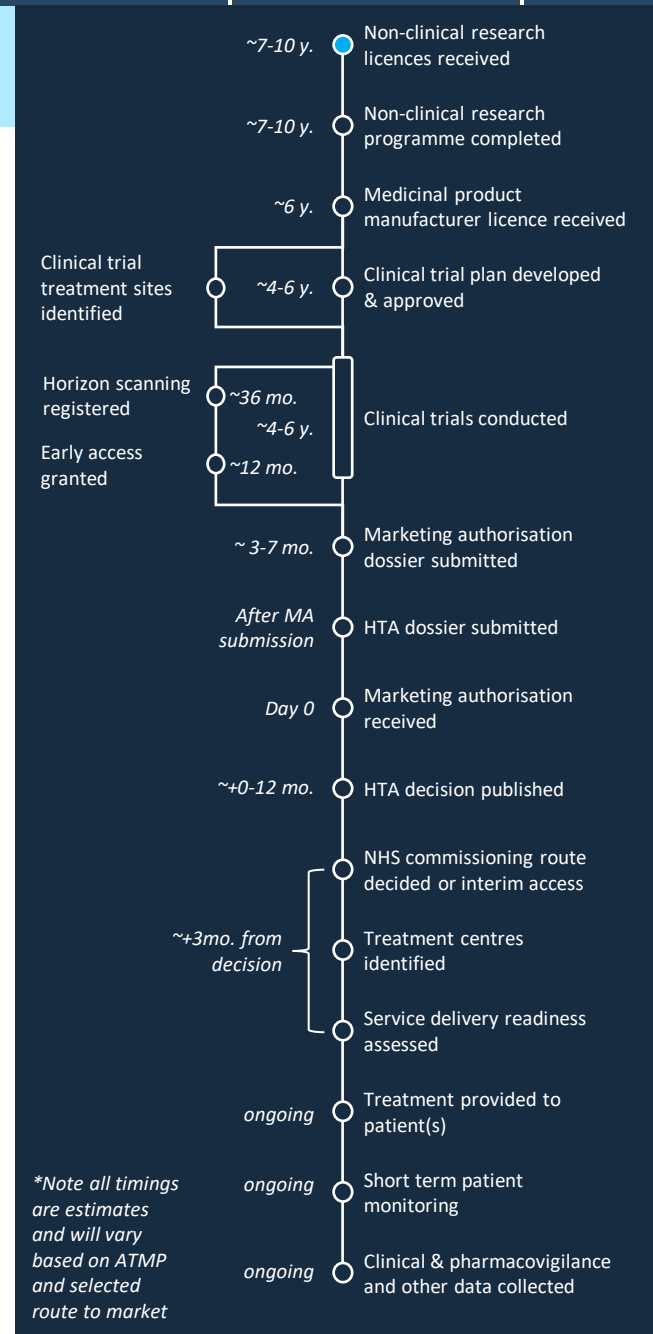
## Overview

## To-do list

## Output

- ATMP developer
- MHRA

**Linked steps** **Who is involved?** **Best practices & tips**



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- Regulatory and/or scientific advice
- **ATMP classification**
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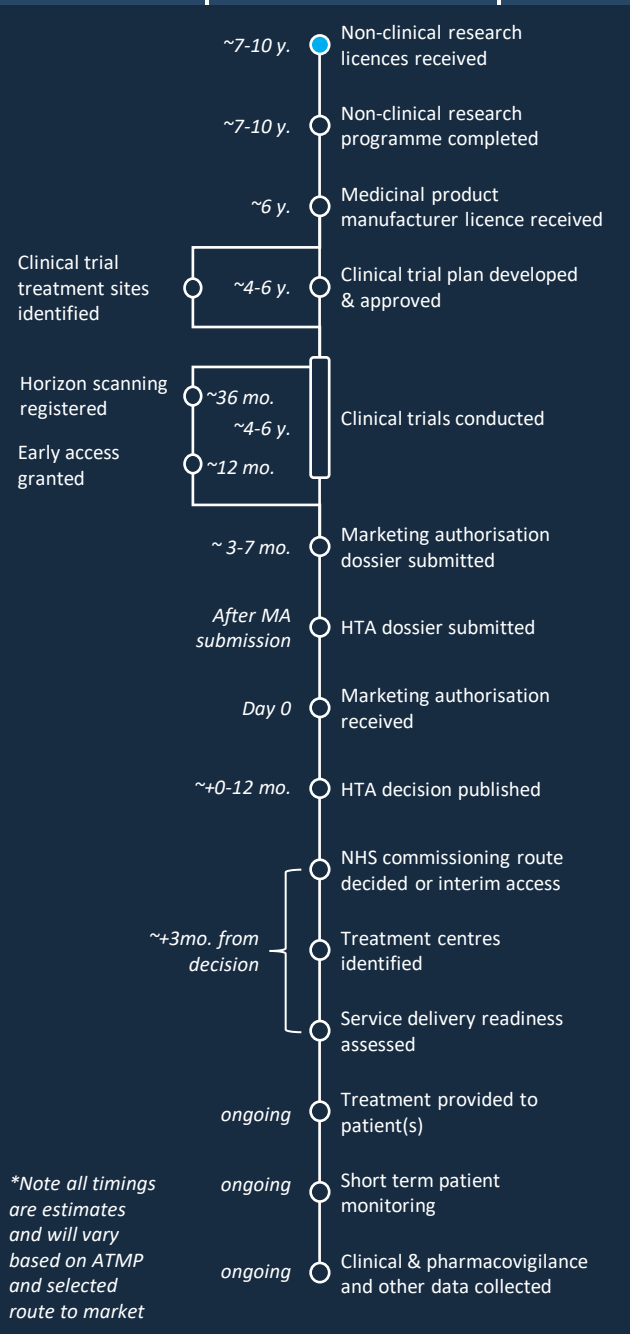
- Manufacturing and supply chain planning

Overview

To-do list

Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- **ATMP quality and non-clinical study requirements**
- Animal model identification & sourcing
- Manufacturing and supply chain planning

**Overview** | To-do list | Output

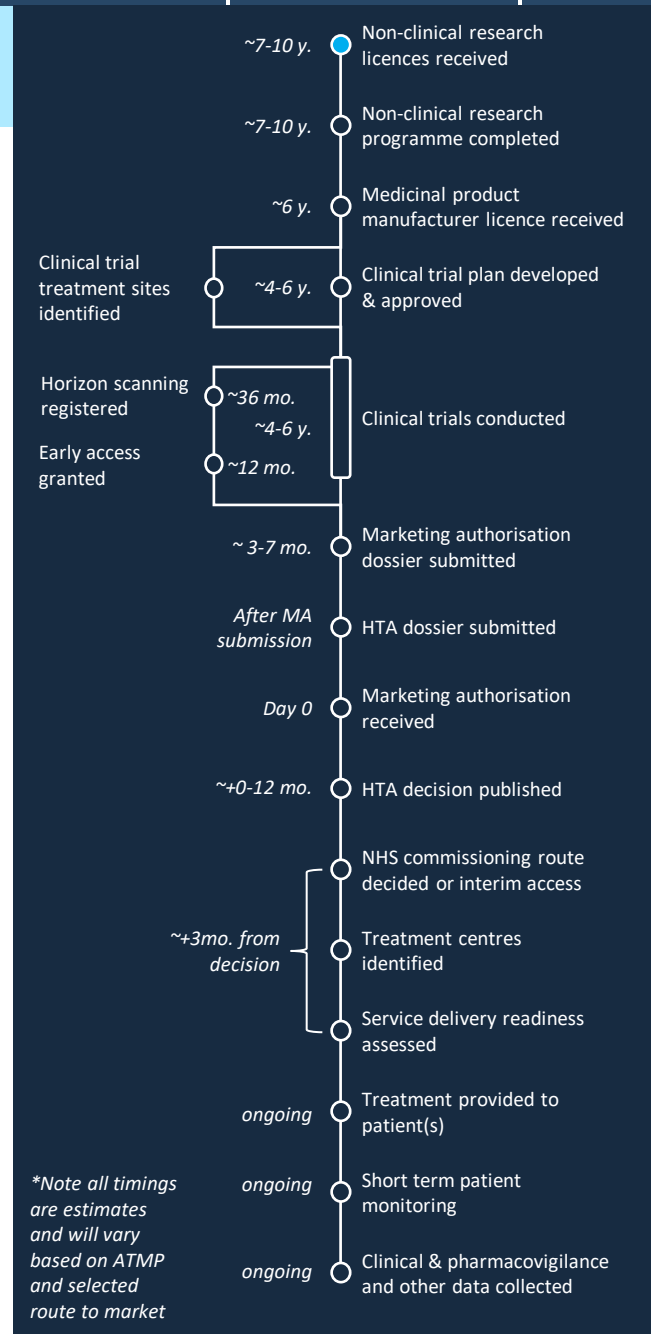
The EMA* has developed quality and non-clinical study requirement guidelines specifically for ATMPs, this guidance is broad and remains useful guidance for UK ATMP developers.
There are two sets of guidelines:

- Gene therapies, and
- Cell therapy and Tissue Engineering

*EMA ATMP specific guidelines are still recommended as a useful source of guidance post-Brexit transition

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- **ATMP quality and non-clinical study requirements**
- Animal model identification & sourcing
- Manufacturing and supply chain planning

Overview | **To-do list** | Output

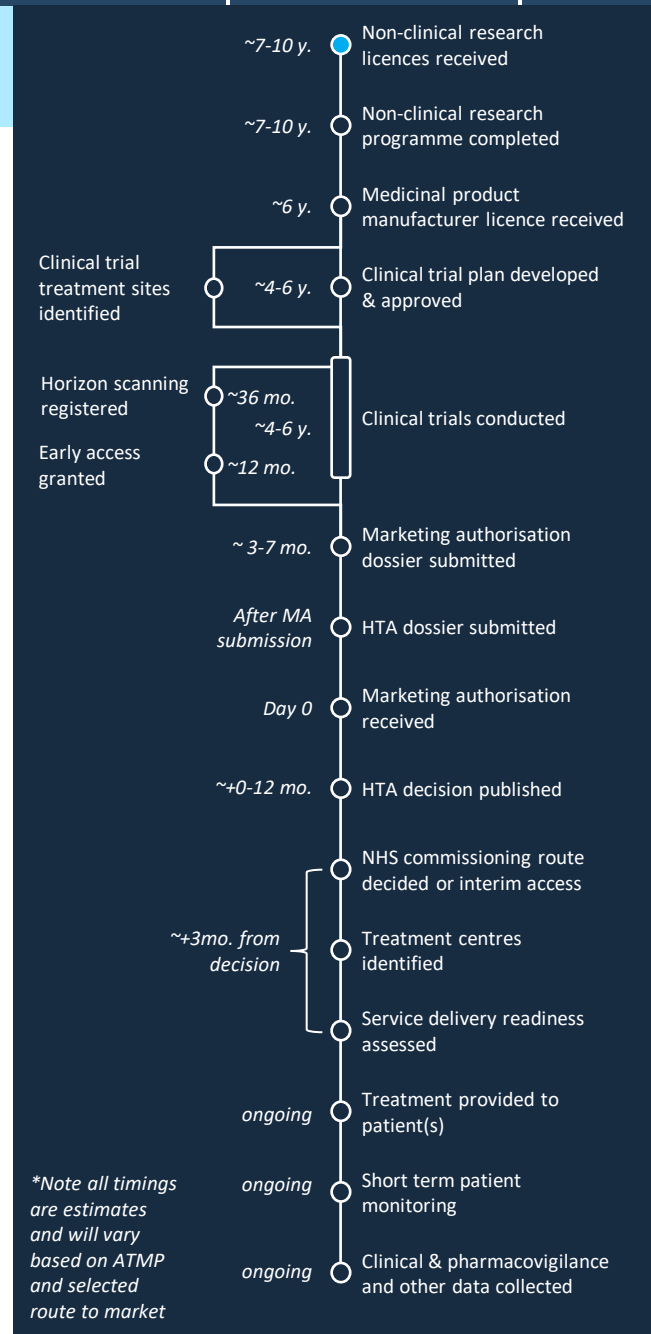
- Review the gene therapy guidelines here
- Review the cell therapy and tissue engineering guidelines here

**When**
Before commencing non-clinical research

*EMA ATMP specific guidelines are still recommended as a useful source of guidance post-Brexit transition

Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**



**1 What advice is available for non-clinical research development?**

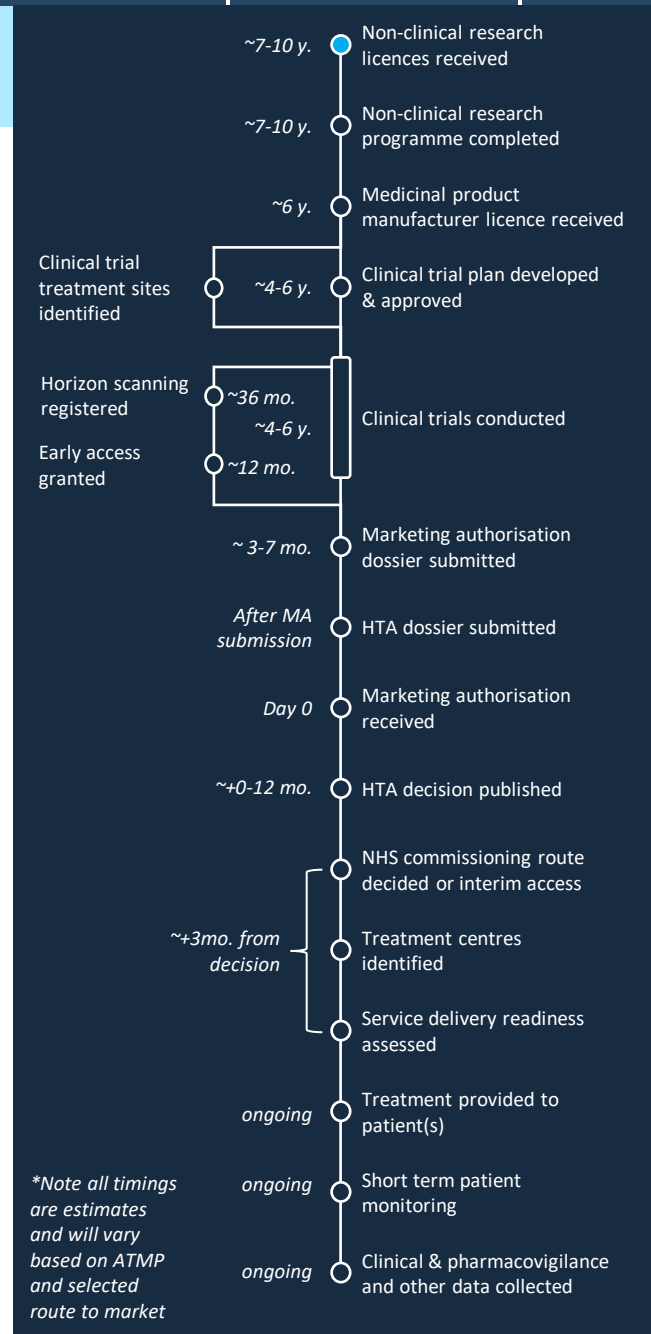
2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- **ATMP quality and non-clinical study requirements**
- Animal model identification & sourcing
- Manufacturing and supply chain planning

Overview | To-do list | **Output**

- For developers of ex-vivo gene therapies it is recommended to review both sets of guidelines




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

# 1 What advice is available for non-clinical research development?

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- **ATMP quality and non-clinical study requirements**
- Animal model identification & sourcing
- Manufacturing and supply chain planning

## Overview

## To-do list

## Output

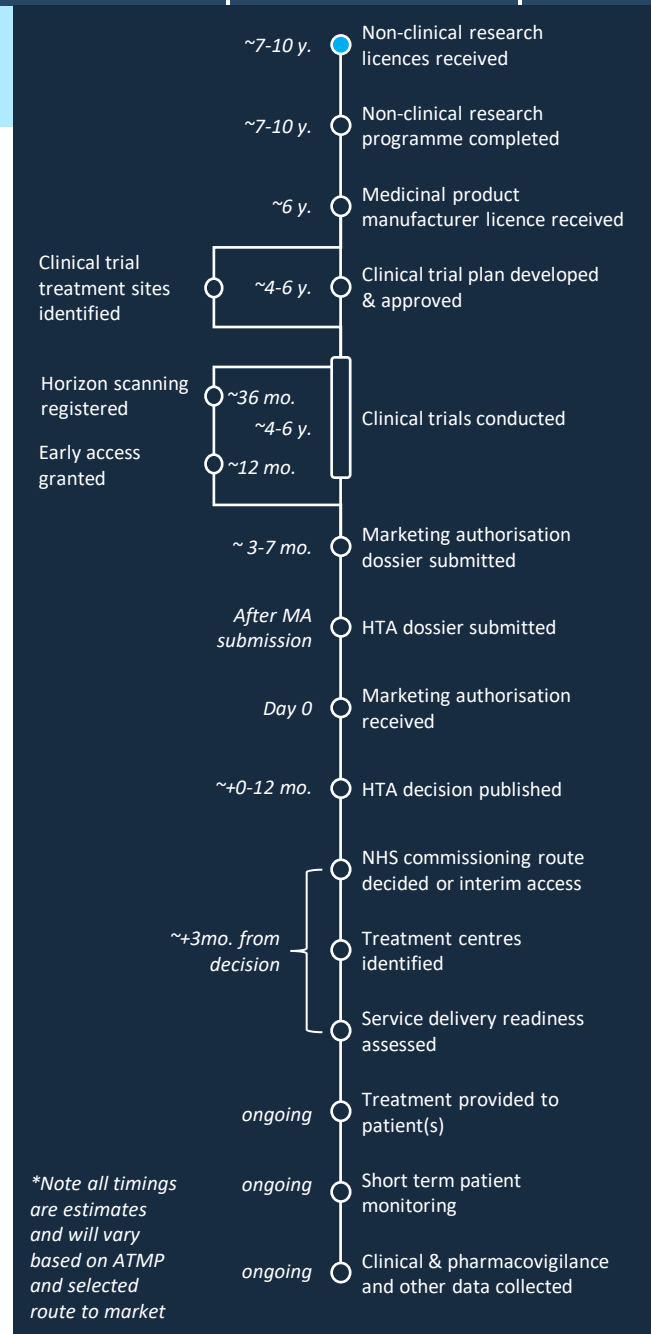
Regulatory and/or scientific advice

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



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## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- **ATMP quality and non-clinical study requirements**
- Animal model identification & sourcing
- Manufacturing and supply chain planning

## Overview

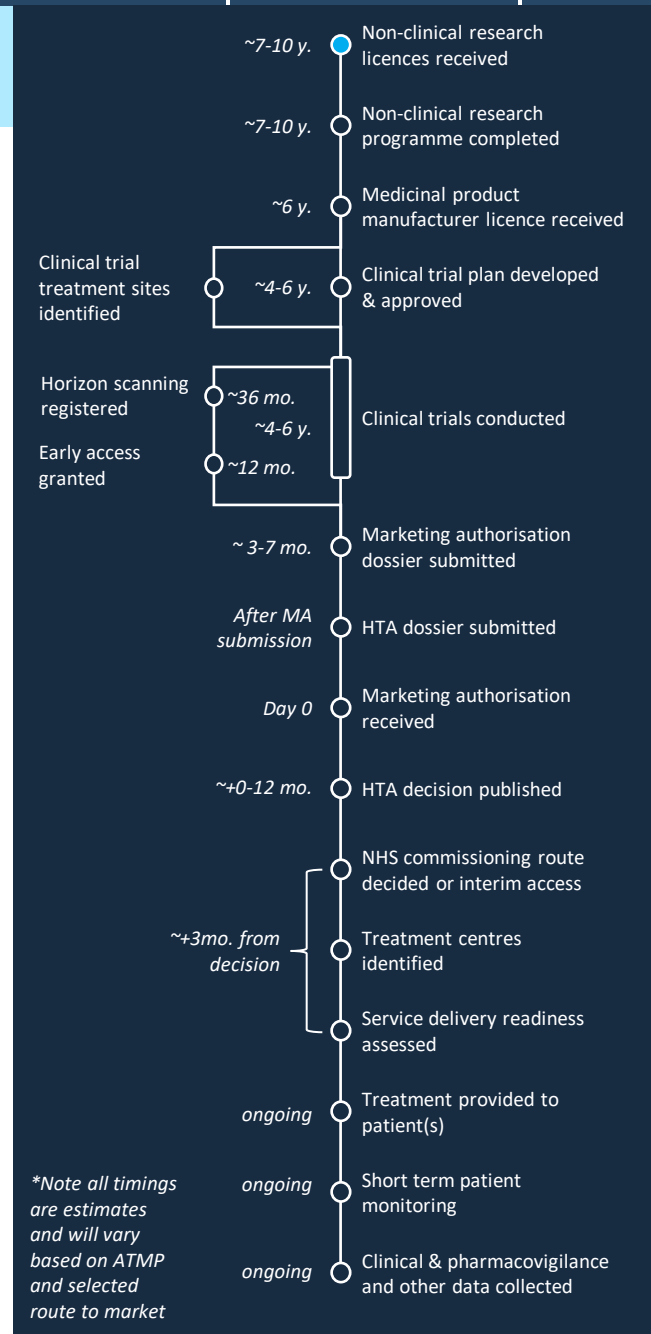
## To-do list

## Output

- ATMP developer

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



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## KEY TOPICS

- Regulatory and/or scientific advice
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- Animal model identification & sourcing
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## Overview

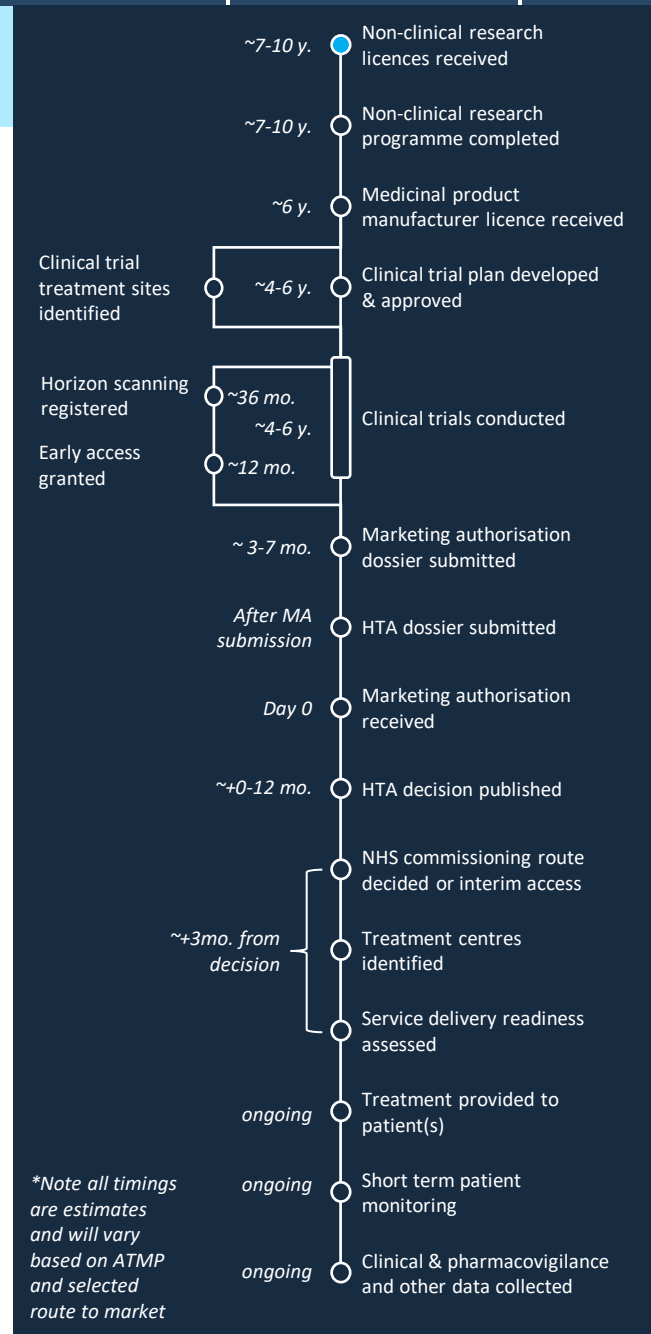
## To-do list

## Output

- For developers of *ex-vivo* gene therapies it is recommended to review both sets of guidelines

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

**Overview** | To-do list | Output

Developers should identify suitable animal models for their ATMP and engage with contract research organisations (CRO) to source.

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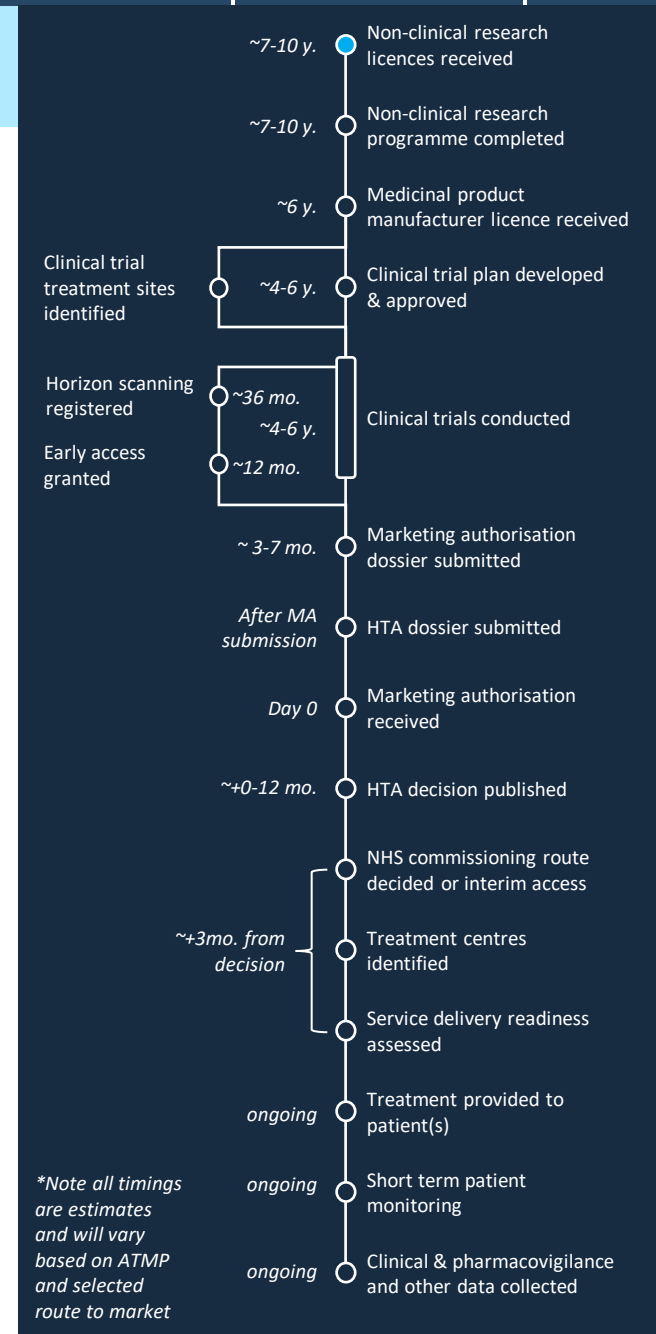

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## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

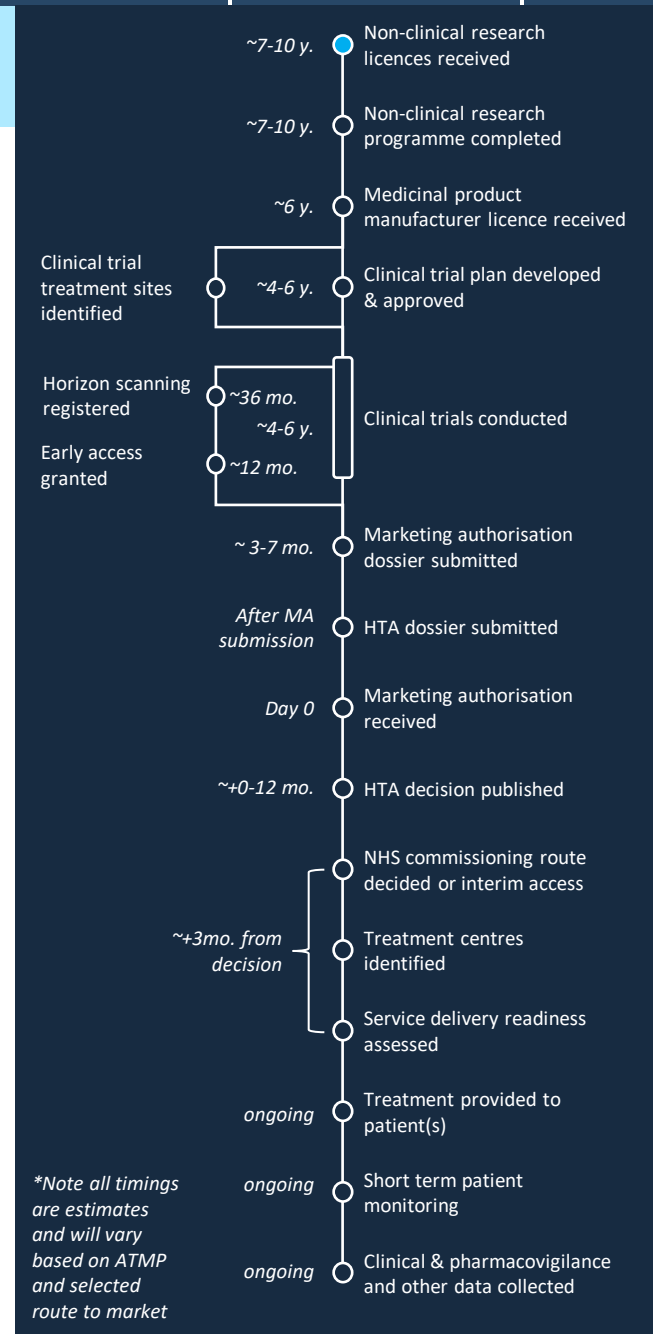
Overview | **To-do list** | Output

- Identify suitable animal models for the ATMP
  - Cell and Gene Therapy Catapult can provide assistance by using the “contact us” feature here
- Engage with contract research organisations to source animal model
- Discuss implications with the MHRA (if applicable), by reaching out to the MHRA Innovation Office here

**When**

Before commencing non-clinical research; engage early to identify and source animal models as the process may take up to 12 months

Linked steps | Who is involved? | Best practices & tips



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

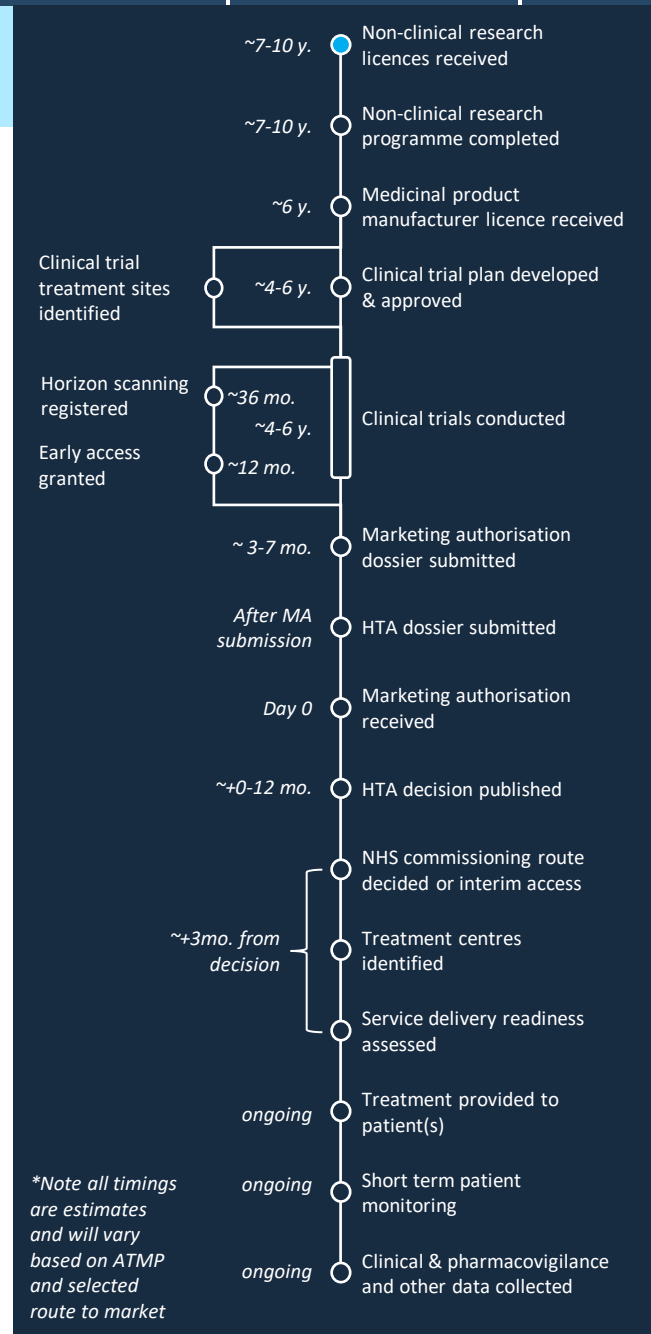
## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

Overview | To-do list | **Output**

- Identified and sourced animal models for ATMP research

Linked steps | Who is involved? | Best practices & tips



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

## Overview

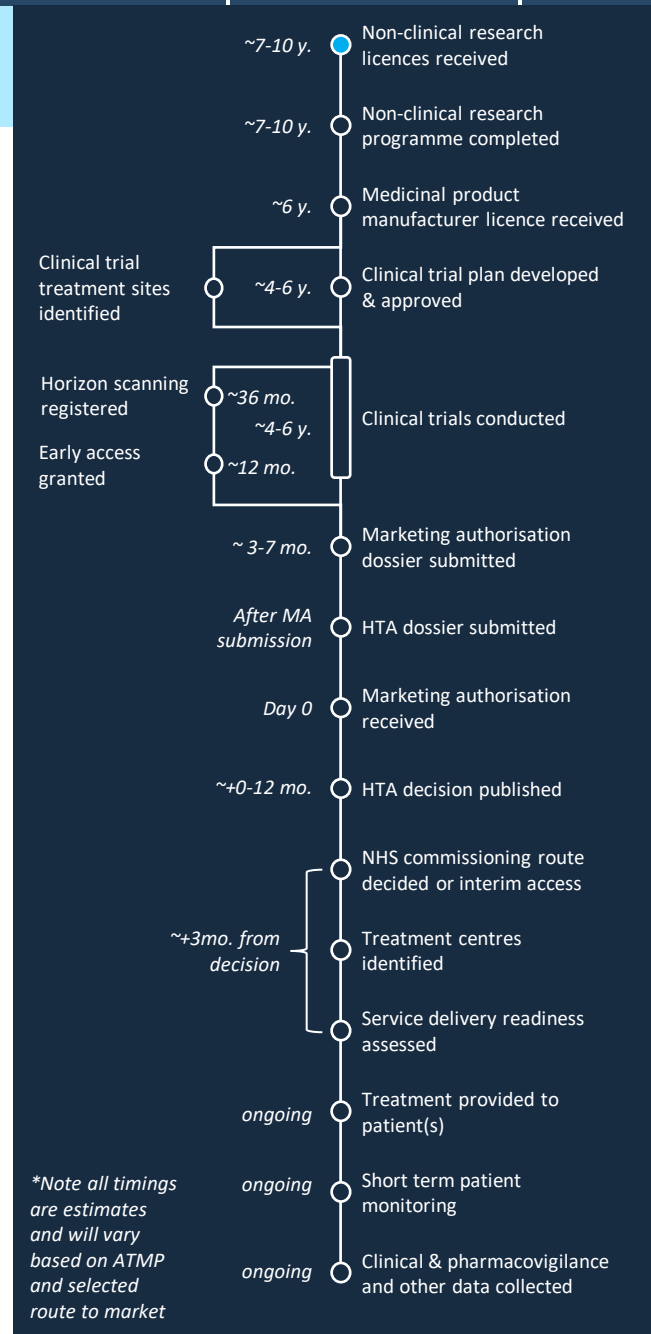
## To-do list

## Output

Regulatory and/or scientific advice

GxP compliance & certification

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

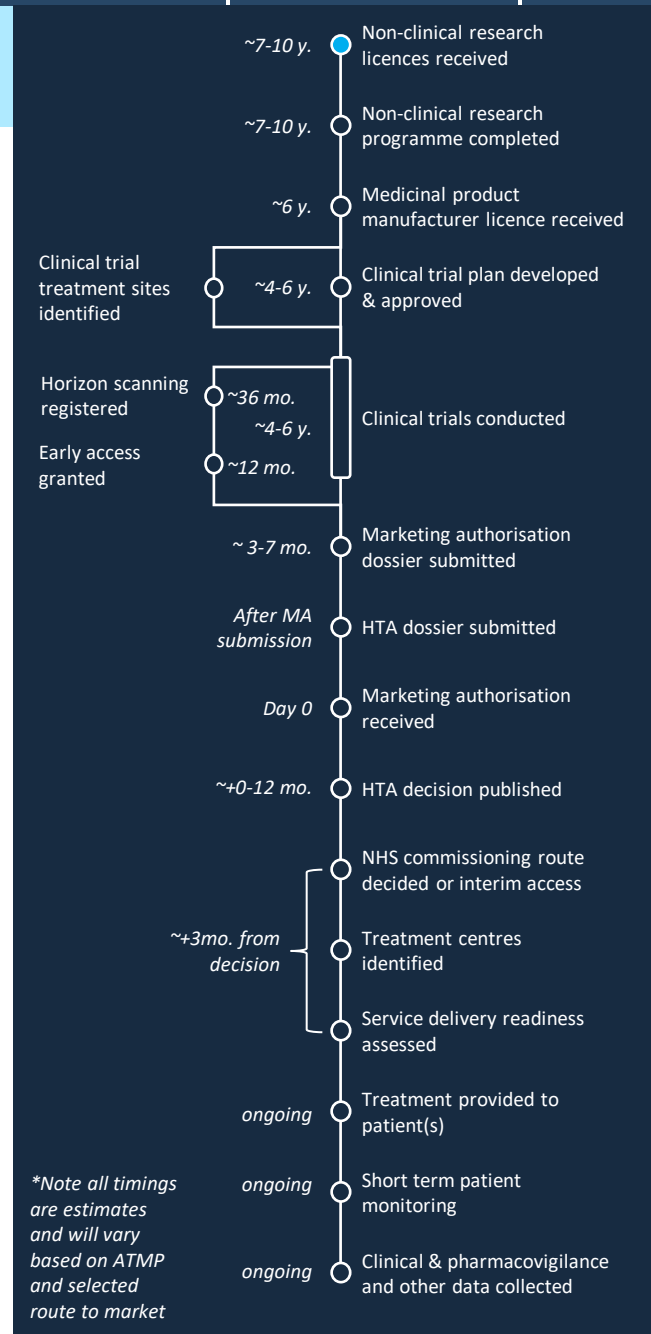
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- CRO

**Linked steps** **Who is involved?** **Best practices & tips**



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2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- **Animal model identification & sourcing**
- Manufacturing and supply chain planning

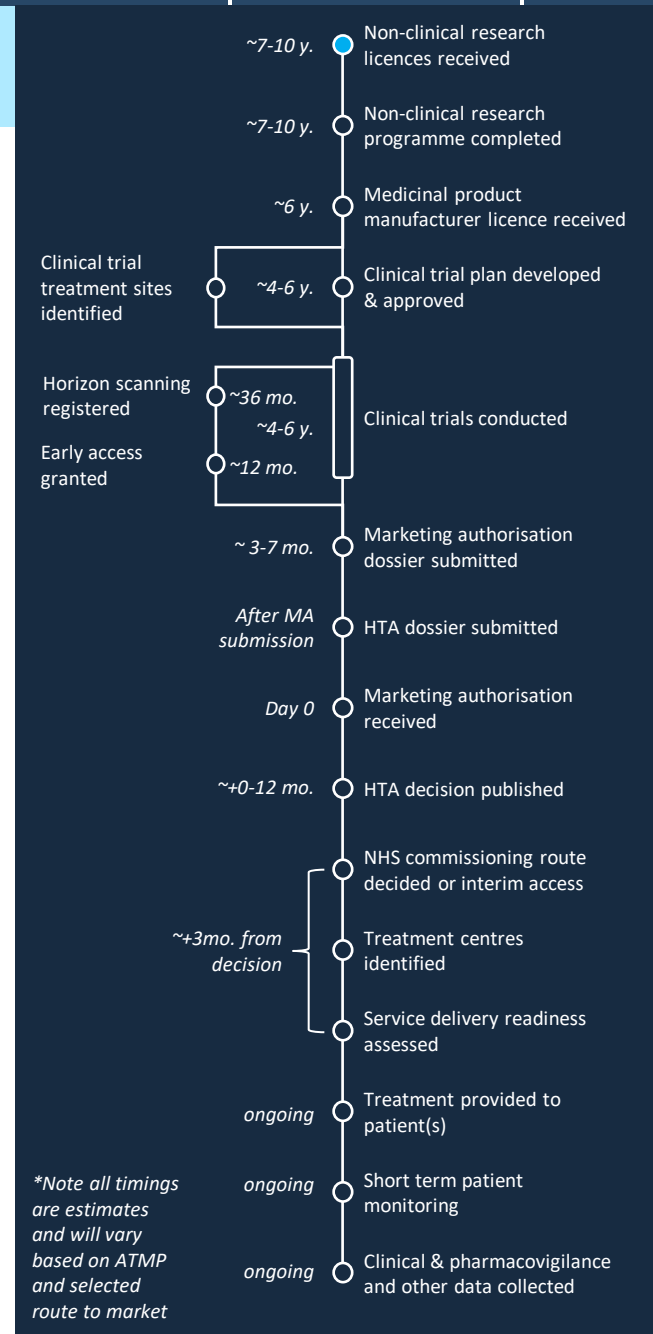
## Overview

## To-do list

## Output

- If planning to perform in-vivo research for an ATMP, identifying and sourcing suitable animal models can be a complex task. It is important to engage early with CROs to source appropriate animals as this can be a time consuming step.

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- **Manufacturing and supply chain planning**

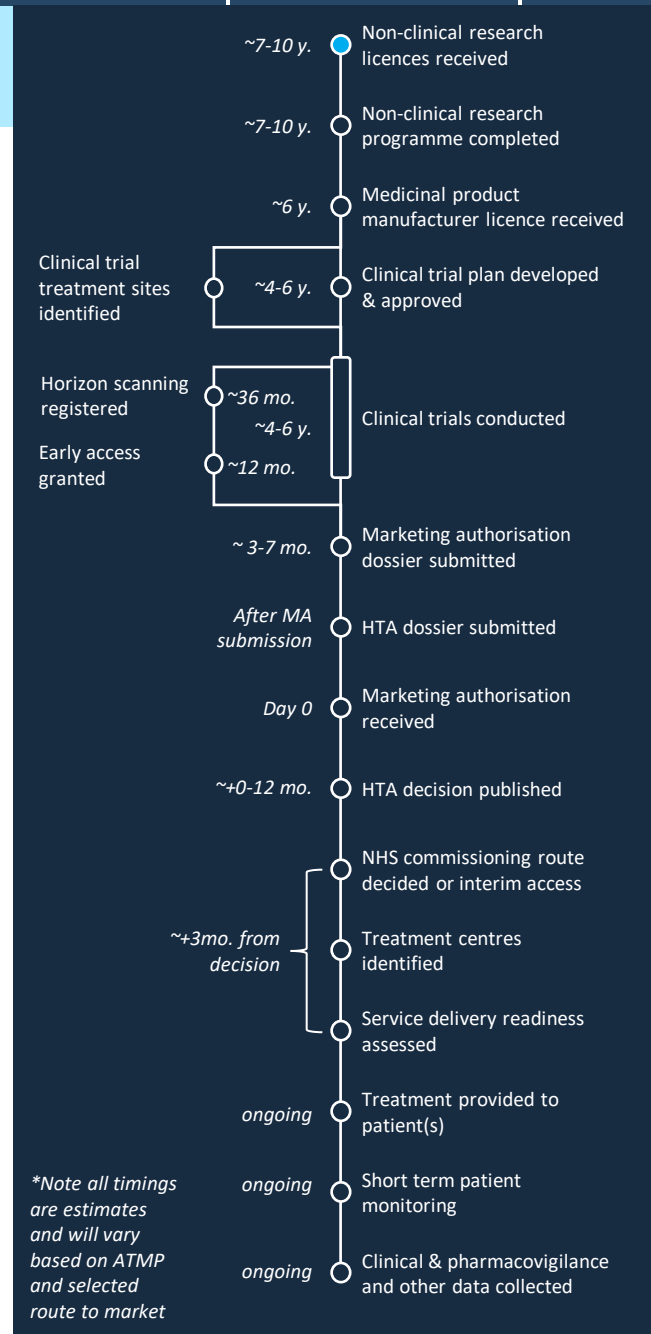
**Overview** | To-do list | Output

Developers should seek support (if required) and conduct manufacturing and supply chain planning, including but not limited to; refrigeration, packaging, courier and labelling requirements.
As part of manufacturing planning, developers should consider the relevant quality control (QC) requirements and determine the assays that will be used for the manufacturing process.

After determining the above, ATMP developers must manufacture the ATMP for use in their research studies, or co-ordinate with a relevant Good Manufacturing Practice (GMP) contractor if this process is being outsourced.

As non-clinical research develops and further data are gathered, developers should ensure that relevant QC and manufacturing processes are updated and developed in line with research findings.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What advice is available for non-clinical research development?**

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## KEY TOPICS

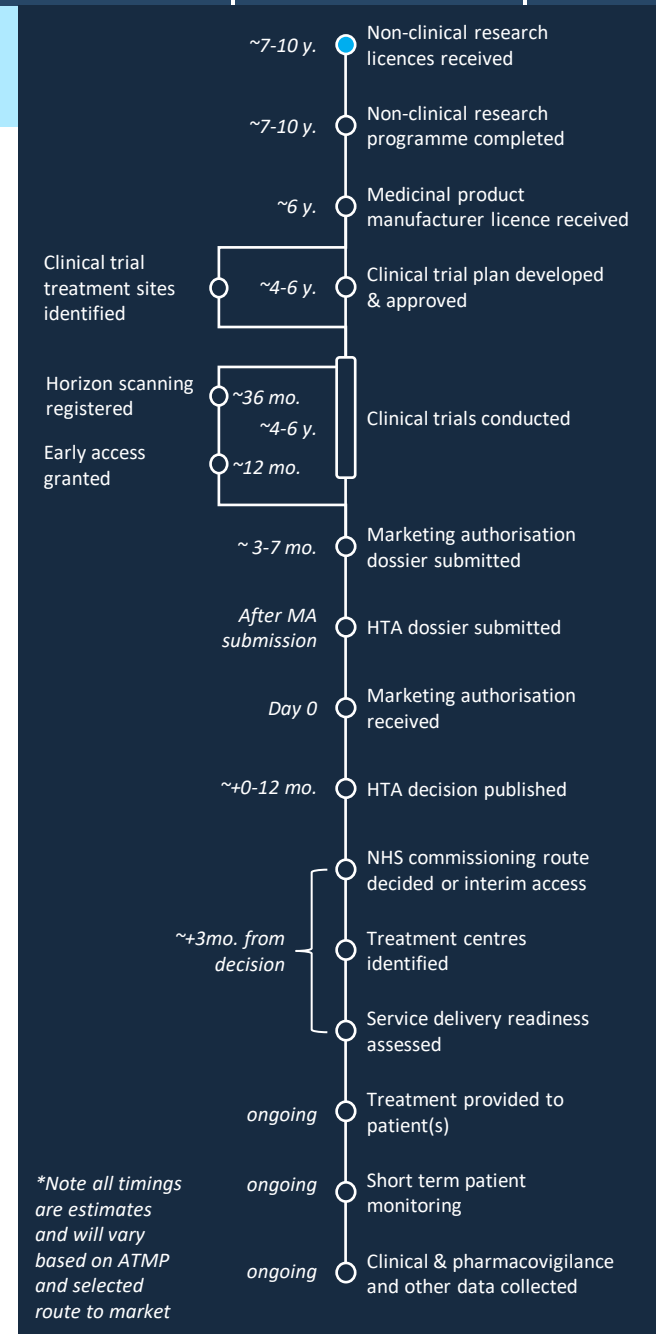
- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- **Manufacturing and supply chain planning**

Overview | **To-do list** | Output

- Review the gene therapy R&D guidelines here
- Review the cell and tissue therapy R&D guidelines here
- Review National Institute of Biological Standards and control standards for bioassays here
- Review guidelines and resources from the EMA on Good Manufacturing Practice in relation to ATMPs here
- Review the Orange Guide and international guidelines from PIC/S here

**When**

During non-clinical research phase, prior to non-clinical study commencement




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

**1 What advice is available for non-clinical research development?**

2 What operational steps are required as part of non-clinical research?

## KEY TOPICS

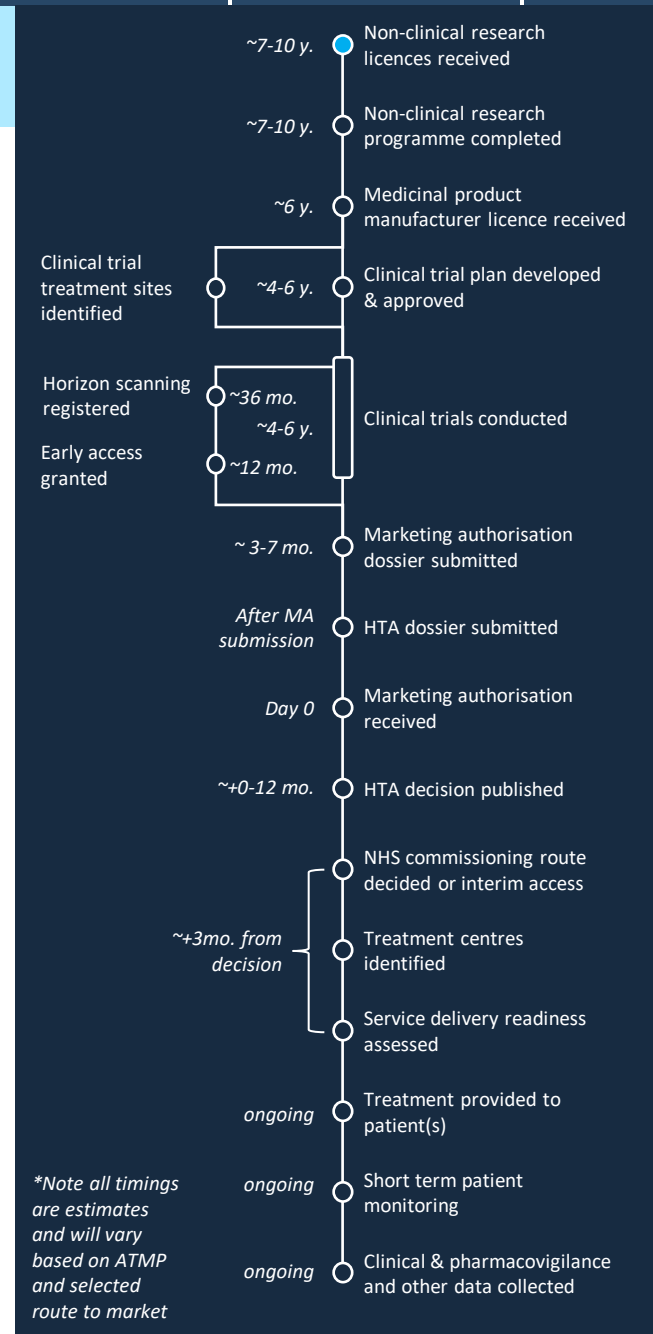
- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- **Manufacturing and supply chain planning**

Overview | To-do list | **Output**

- Planning documentation for manufacture and supply chain
- Quality control requirements

Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**



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## KEY TOPICS

- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- **Manufacturing and supply chain planning**

## Overview

## To-do list

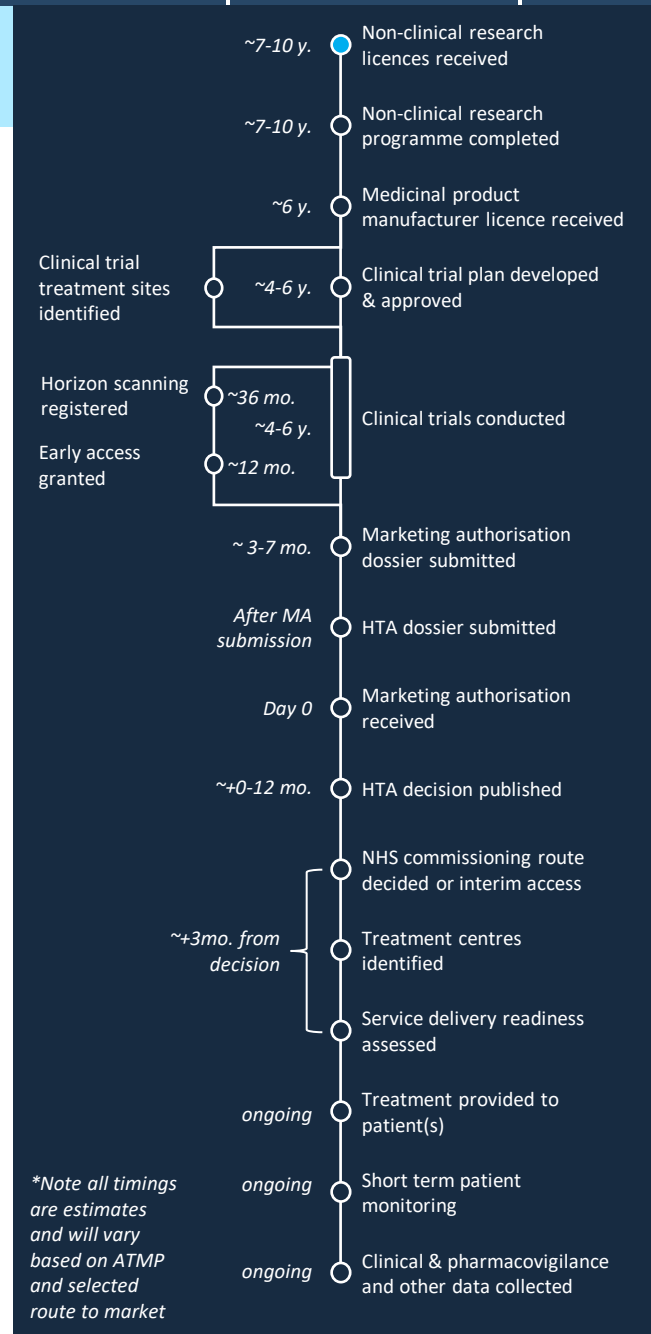
## Output

Regulatory and/or scientific advice

GxP compliance & certification

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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- Regulatory and/or scientific advice
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## Overview

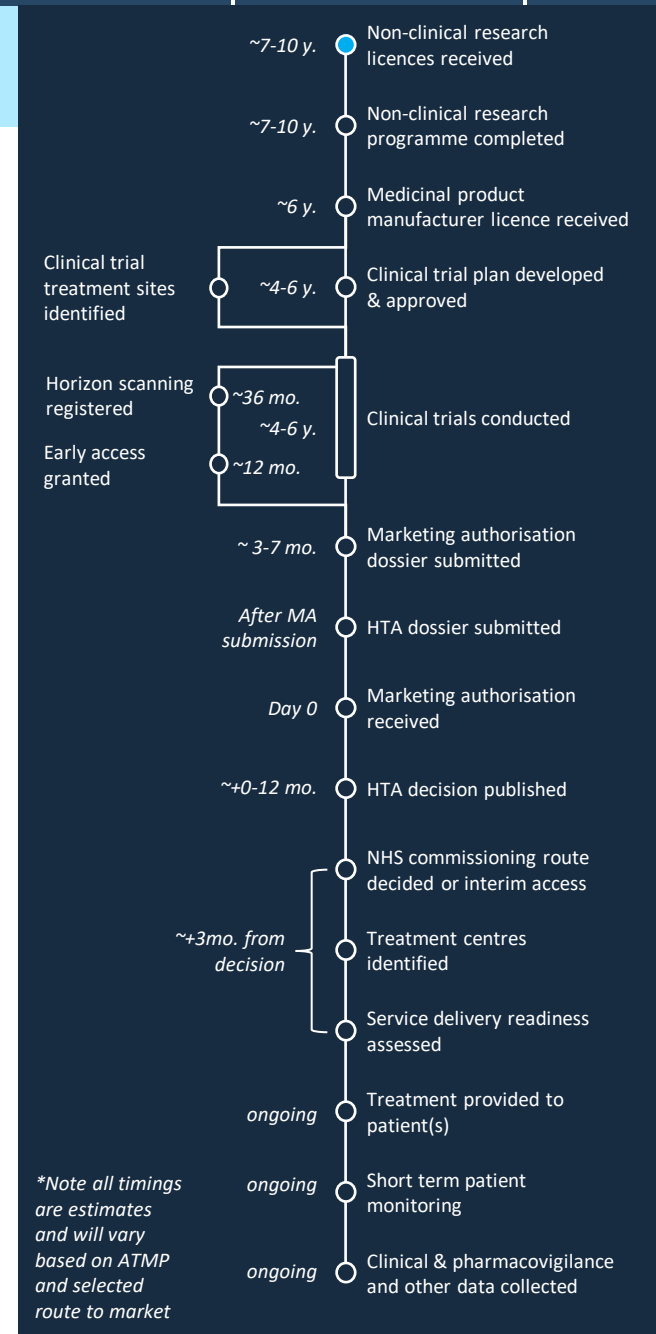
## To-do list

## Output

- ATMP developer

Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**



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## KEY TOPICS

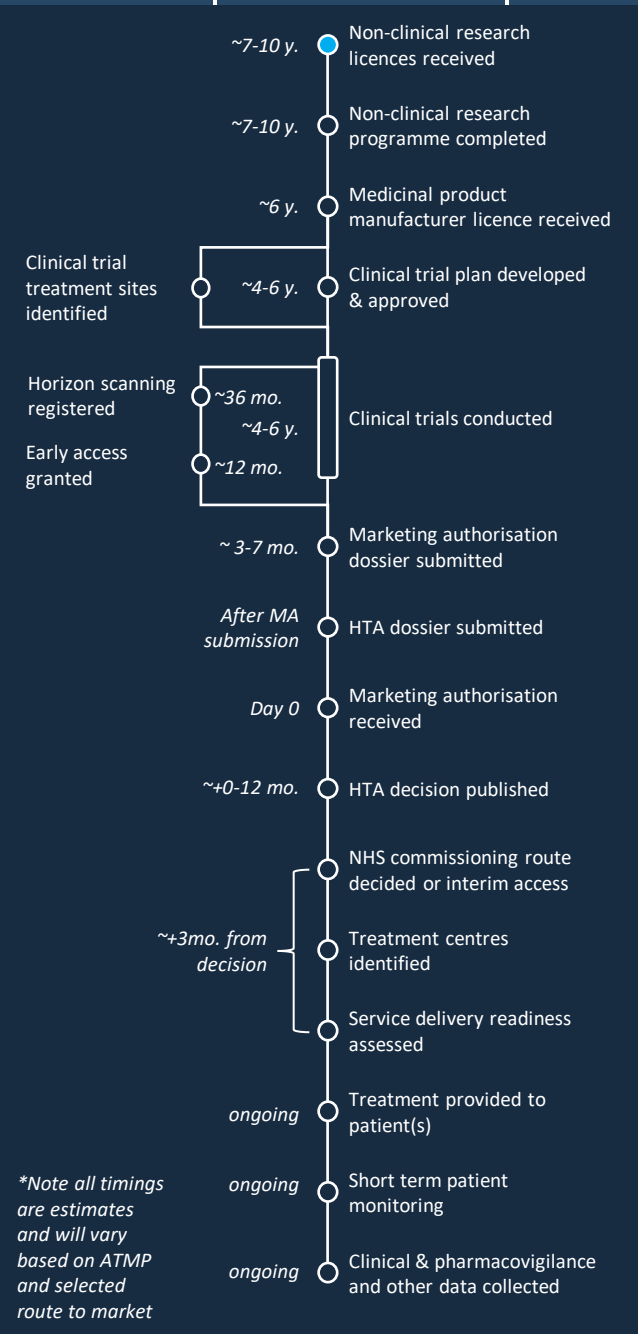
- Regulatory and/or scientific advice
- ATMP classification
- ATMP quality and non-clinical study requirements
- Animal model identification & sourcing
- **Manufacturing and supply chain planning**

## Overview

## To-do list

## Output

- Developers should ensure that the manufacturing and supply chain processes are updated as and when developments occur, during both non-clinical and clinical research
- If using a sub-contracted manufacturer, ensure that all relevant contractual agreements are in place
- Developers are recommended to review guidance from SPS on product design considerations for optimising ATMP implementation in the NHS here




Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype

1 What advice is available for non-clinical research development?

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## KEY TOPICS

- **Animal model identification & sourcing**
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

**Overview** | To-do list | Output

Developers should identify suitable animal models for their ATMP and engage with Contract Research Organisations (CRO) to source.

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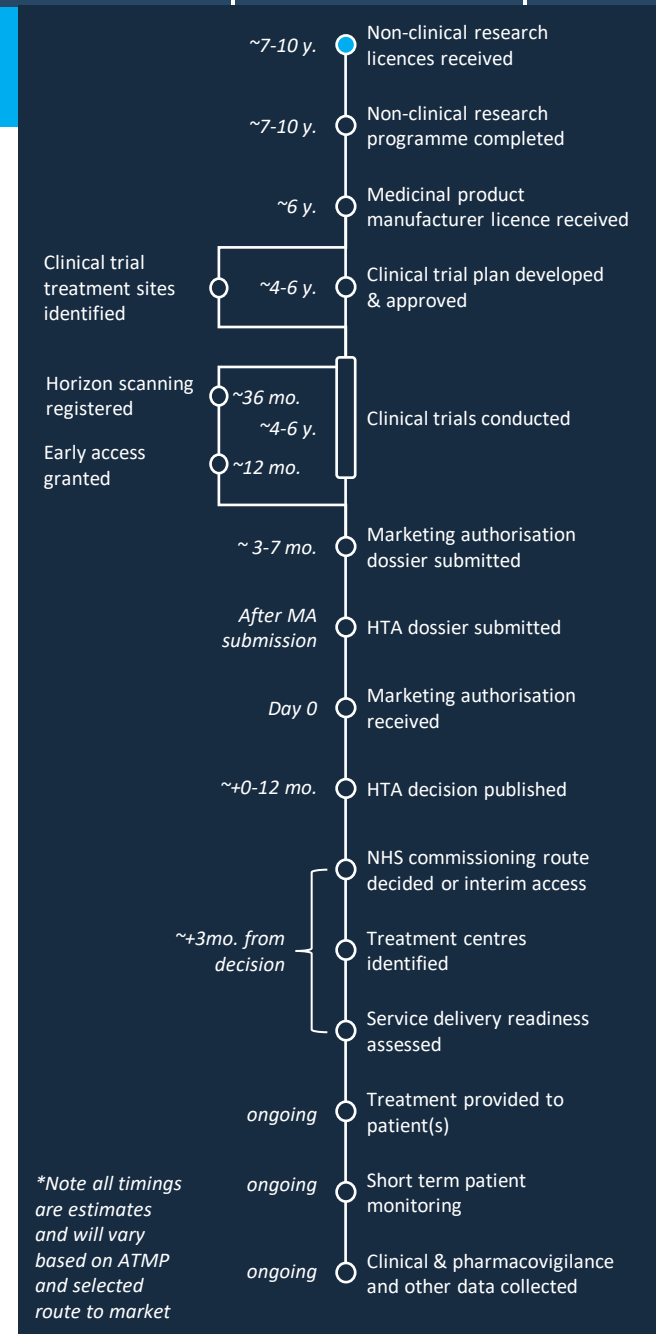

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## KEY TOPICS

- **Animal model identification & sourcing**
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Overview | **To-do list** | Output

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**When**

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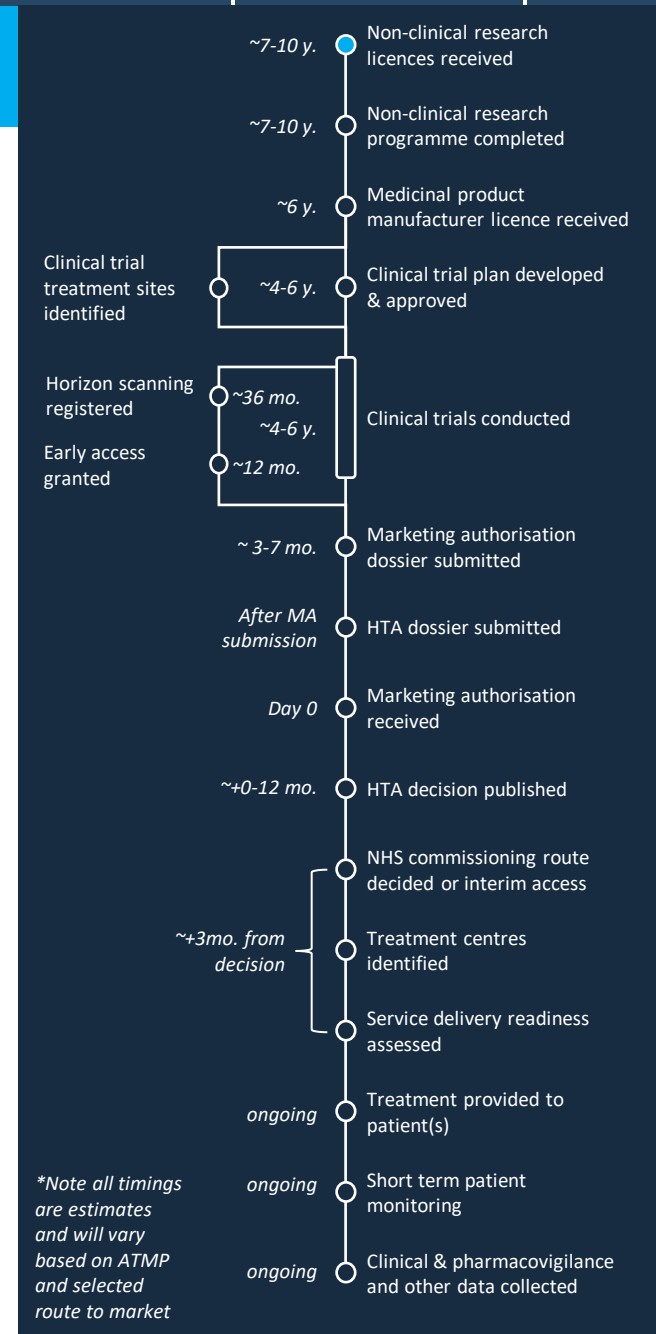
Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- **Animal model identification & sourcing**
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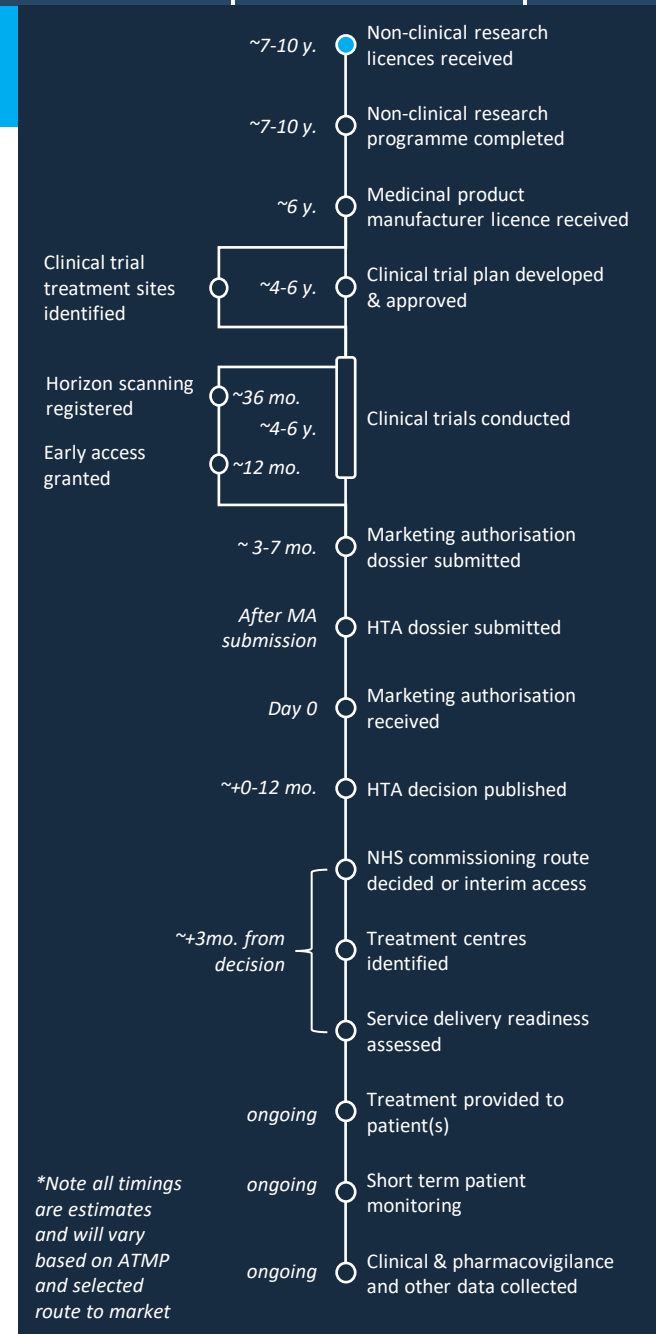
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

Overview | To-do list | **Output**

- Identified and sourced animal models for ATMP research

**Linked steps** | **Who is involved?** | **Best practices & tips**



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## Overview

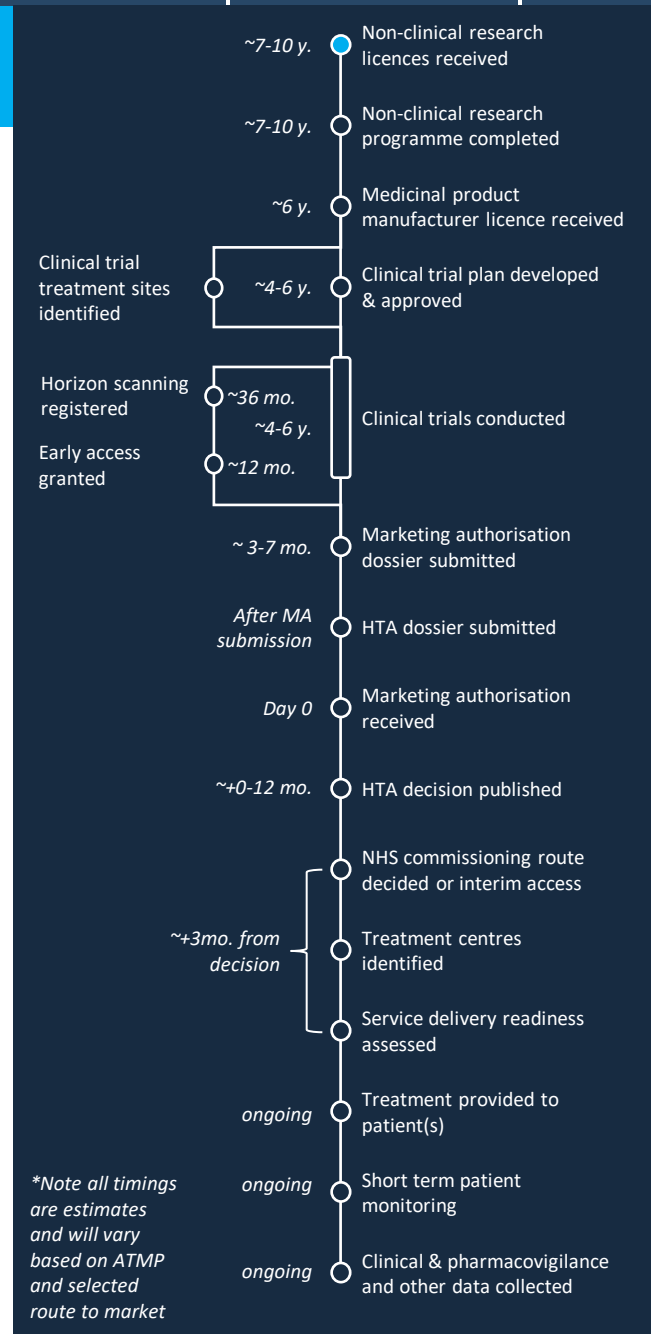
## To-do list

## Output

Regulatory and/or scientific advice

GxP compliance & certification

**Linked steps** **Who is involved?** **Best practices & tips**



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- **Animal model identification & sourcing**
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

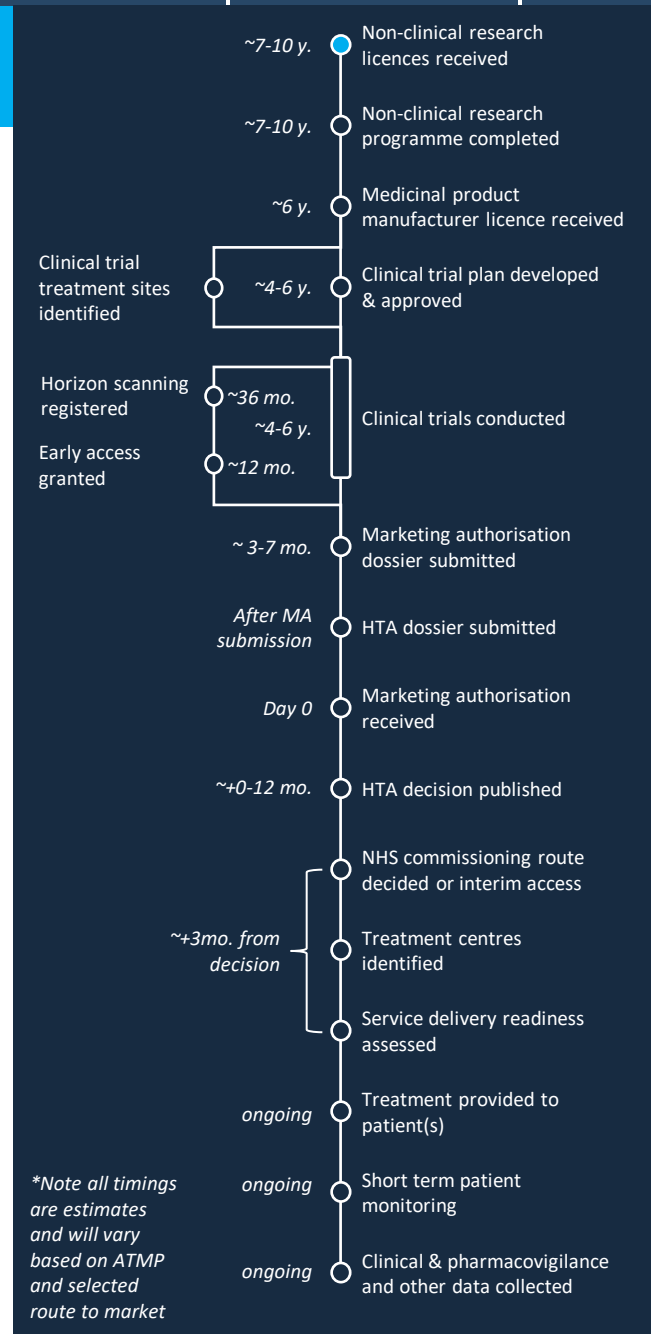
## Overview

- ATMP developer
- MHRA
- CRO

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- **Animal model identification & sourcing**
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
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## Overview

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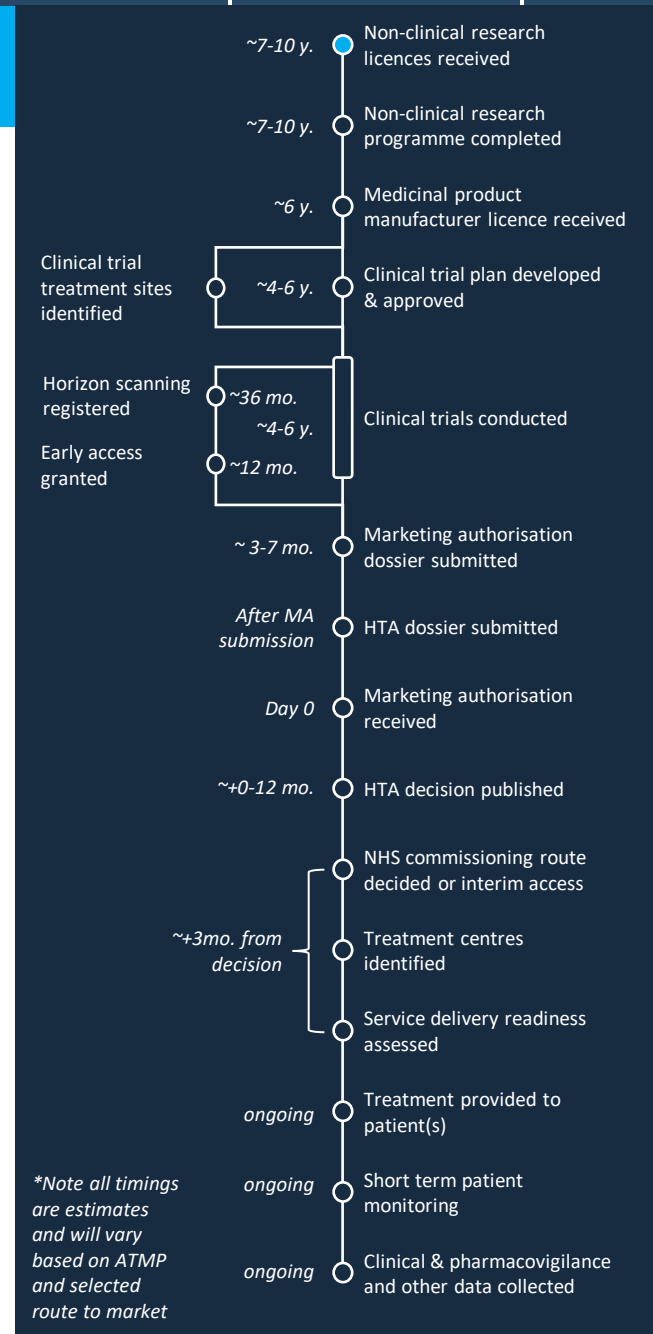
## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

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- *In vitro* and *in vivo* studies
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**Overview** | To-do list | Output

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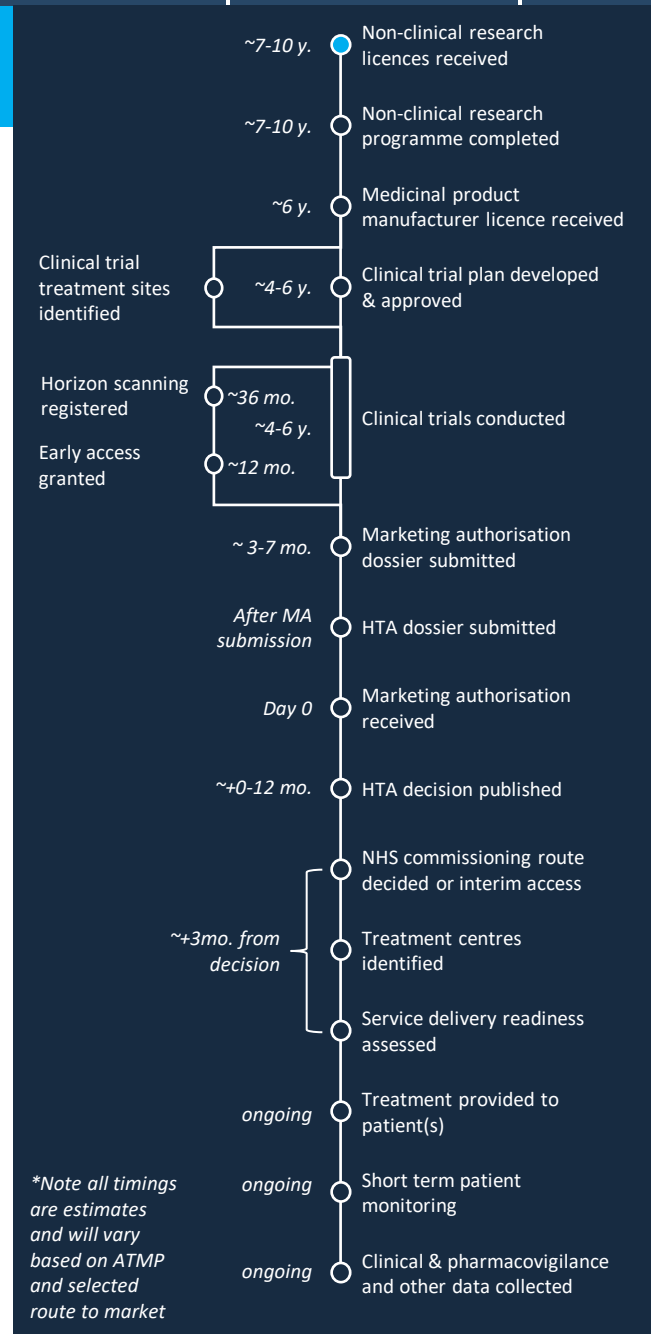
Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



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## KEY TOPICS

- Animal model identification & sourcing
- **Manufacturing and supply chain planning**
- *In vitro* and *in vivo* studies
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Overview | **To-do list** | Output

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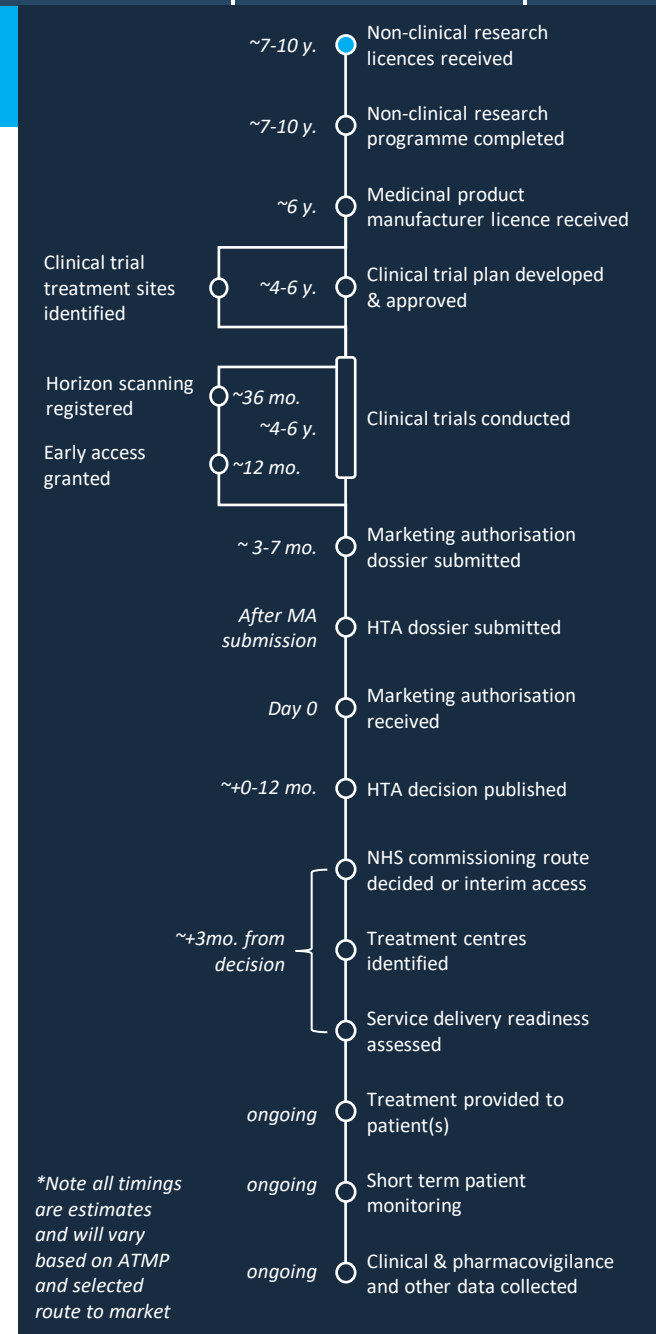
**When**

During non-clinical research phase, prior to non-clinical study commencement

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



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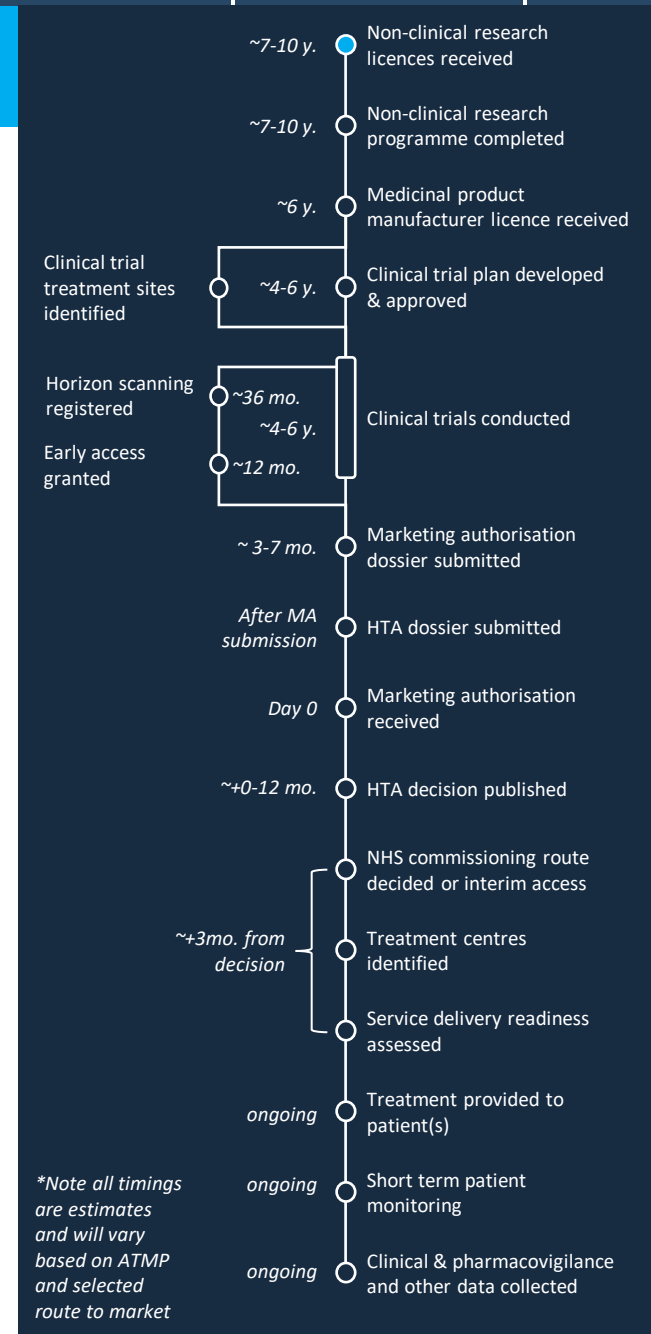
## KEY TOPICS

- Animal model identification & sourcing
- **Manufacturing and supply chain planning**
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

Overview | To-do list | **Output**

- Planning documentation for manufacture and supply chain
- Quality control requirements




Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**

1 What advice is available for non-clinical research development?

**2 What operational steps are required as part of non-clinical research?**

## KEY TOPICS

- Animal model identification & sourcing
- **Manufacturing and supply chain planning**
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
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## Overview

## To-do list

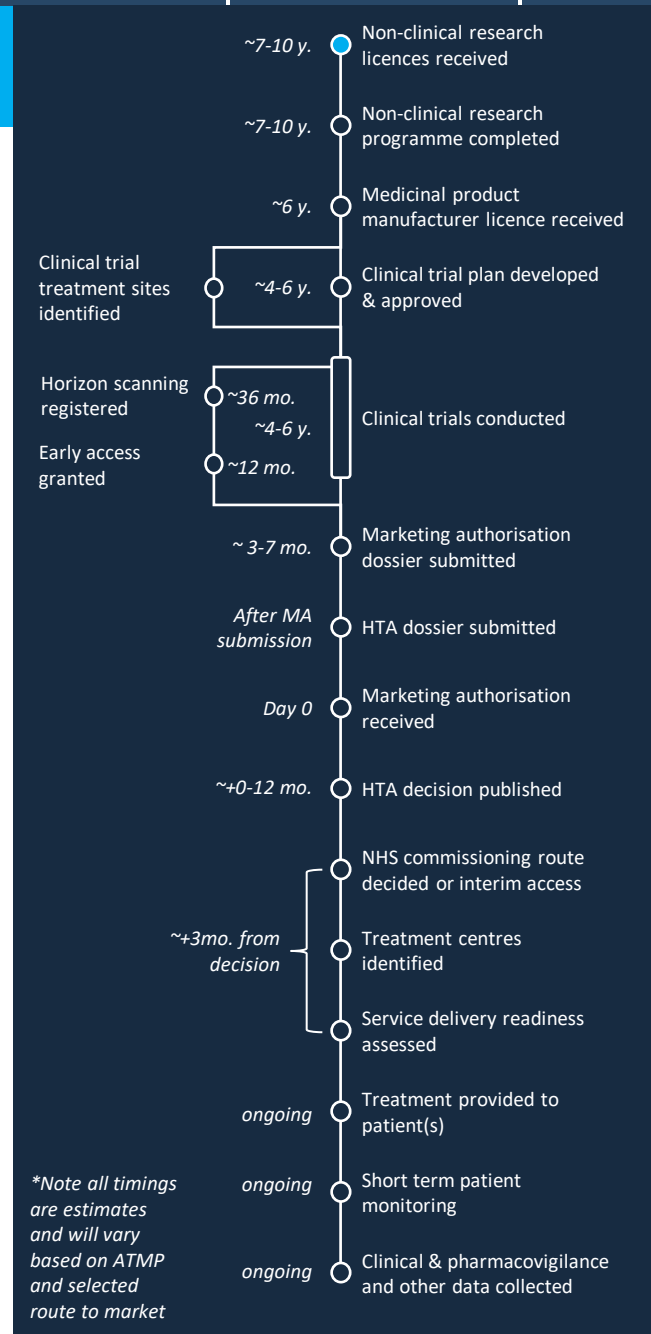
## Output

Regulatory and/or scientific advice

GxP compliance & certification

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



1 What advice is available for non-clinical research development?

**2 What operational steps are required as part of non-clinical research?**

## KEY TOPICS

- Animal model identification & sourcing
- **Manufacturing and supply chain planning**
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

## Overview

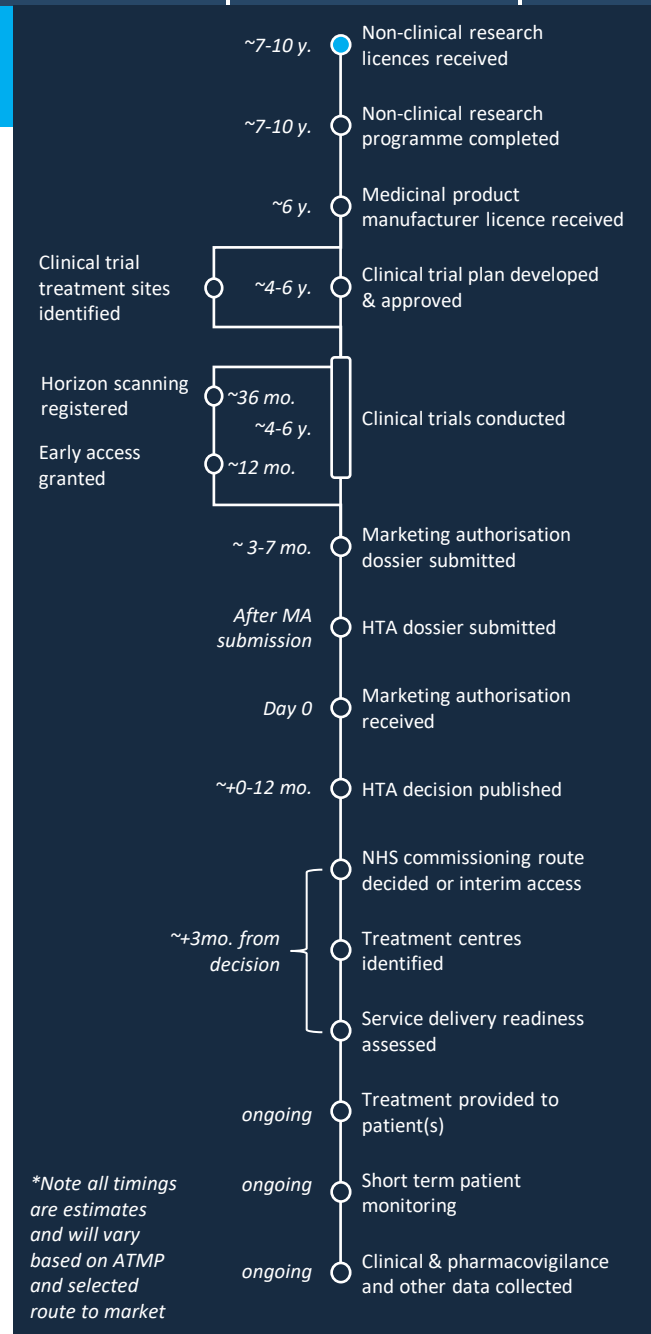
- ATMP developer

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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## KEY TOPICS

- Animal model identification & sourcing
- **Manufacturing and supply chain planning**
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- Research documentation consolidation

## Overview

## To-do list

## Output

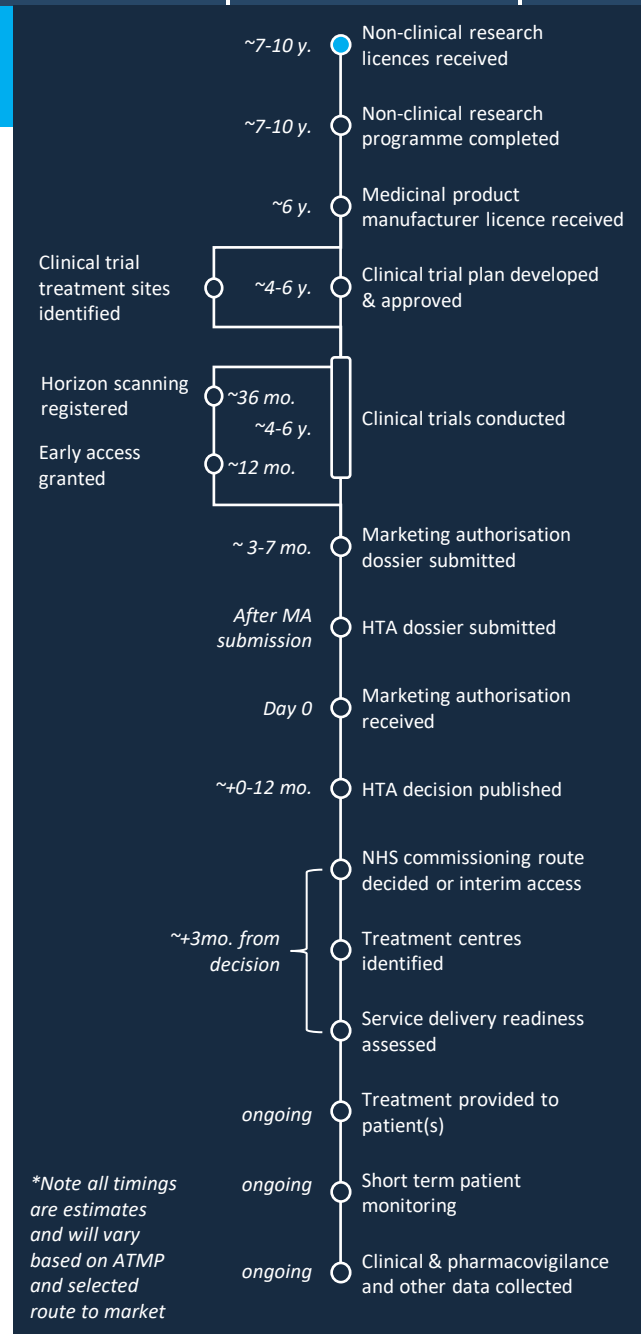
- Developers should ensure that the manufacturing and supply chain processes are updated as and when developments occur, during both non-clinical and clinical research
- If using a sub-contracted manufacturer, ensure that all relevant contractual agreements are in place
- Developers are recommended to review guidance from SPS on product design considerations for optimising ATMP implementation in the NHS here


Linked steps


Who is involved?


Best practices & tips


Variation by ATMP archetype



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- ***In vitro* and *in vivo* studies**
- Delivery and diagnostic route assessment
- Research documentation consolidation

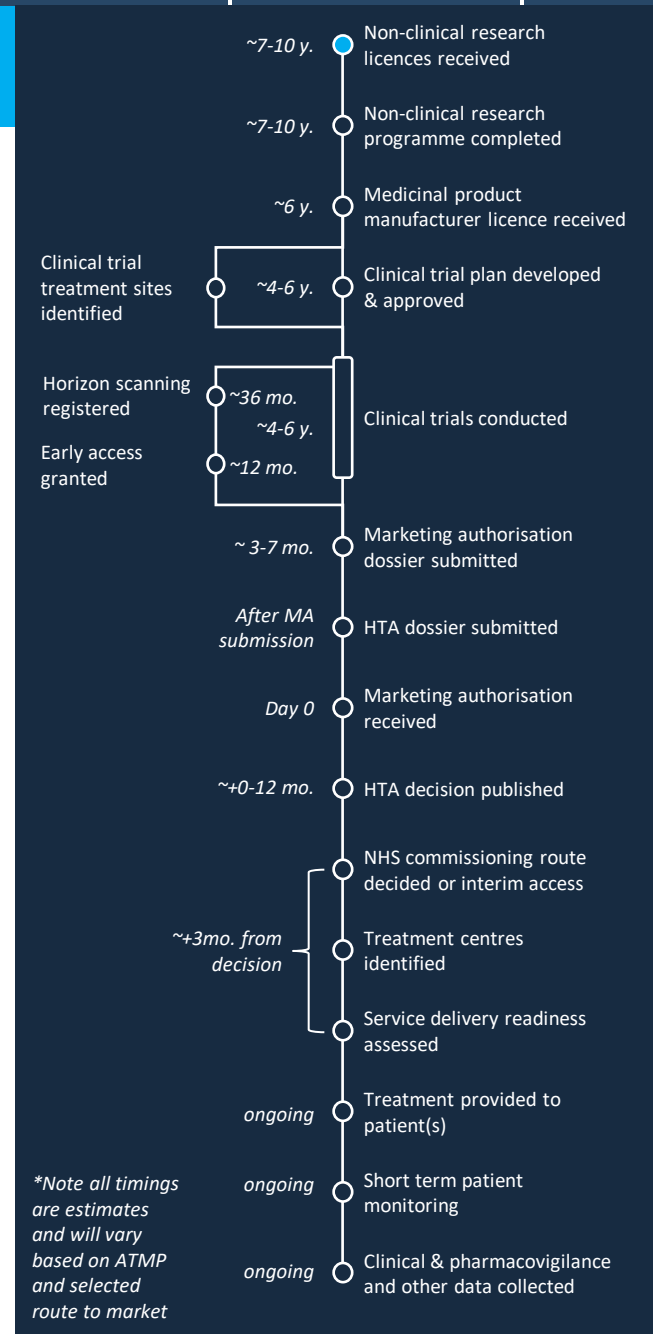
**Overview** | To-do list | Output

Before commencing *in vitro* research, developers must document *in vitro* research study design (this should include a detailed risk assessment). The *in vitro* studies should assess the safety risks and impact of the substance. If applicable, publish *in vitro* study results in a peer-reviewed journal. Once *in vitro* studies are complete (if applicable), developers should design, perform and publish their *in vivo* studies.

Note: ATMP developers may choose not to perform *in vitro* or *in vivo* studies if there are limitations based on their ATMP type, however if these are not performed developers should be able to provide requisite safety evidence and justification for this decision. ATMP developers should consult with the MHRA to identify the appropriate toxicology tests expected.

As non-clinical research progresses, developers should ensure to update any processes related to manufacturing, quality control and documentation related to these processes (including any patent applications if applicable).

Linked steps | Who is involved? | Best practices & tips



1 What advice is available for non-clinical research development?

**2 What operational steps are required as part of non-clinical research?**

## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- ***In vitro* and *in vivo* studies**
- Delivery and diagnostic route assessment
- Research documentation consolidation

Overview | **To-do list** | Output

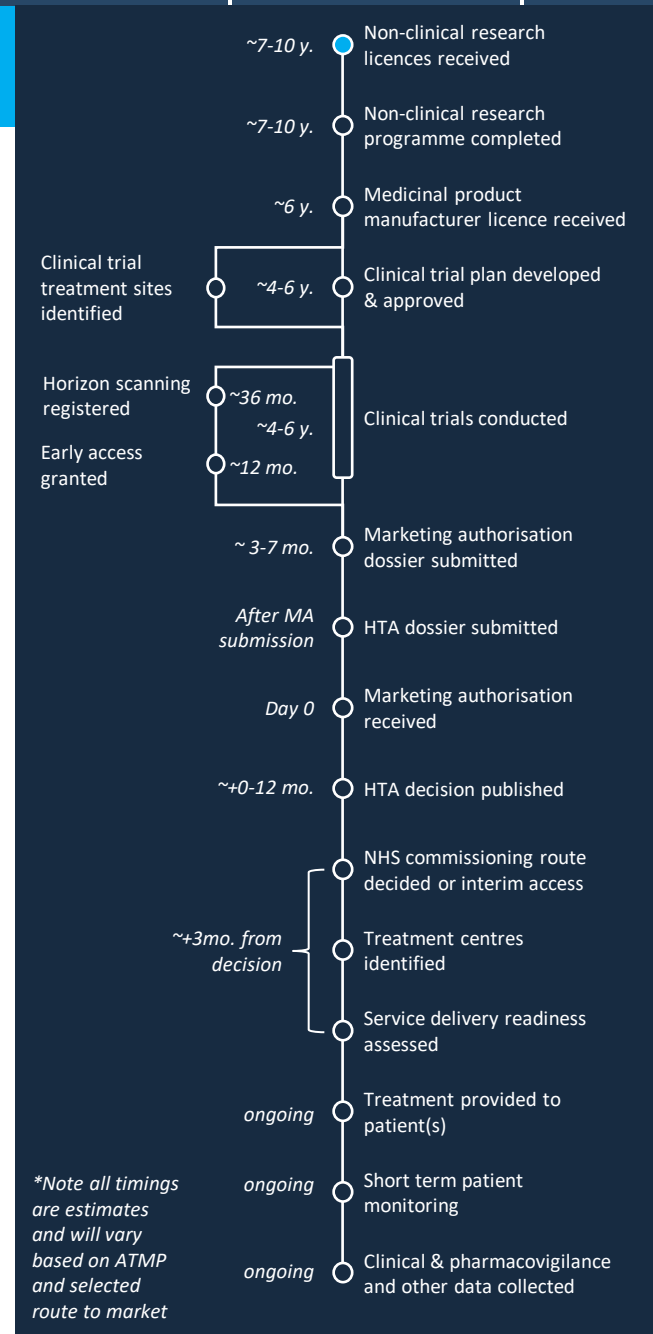
- Conduct environmental risk assessment for non-clinical research
  - EMA* guidance can be found here
- Request advice from the MHRA to identify appropriate toxicology tests
- Document *in vitro* study design (including risk assessment)
- Perform *in vitro* studies and publish study results
- Document *in vivo* study design (including risk assessment)
- Perform *in vivo* studies and publish study results
- Review existing patent application (if applicable) and identify if any updates required through guidance here

**When**

During non-clinical research phase

*EMA ATMP specific guidelines are still recommended as a useful source of guidance post-Brexit transition

Linked steps | Who is involved? | Best practices & tips



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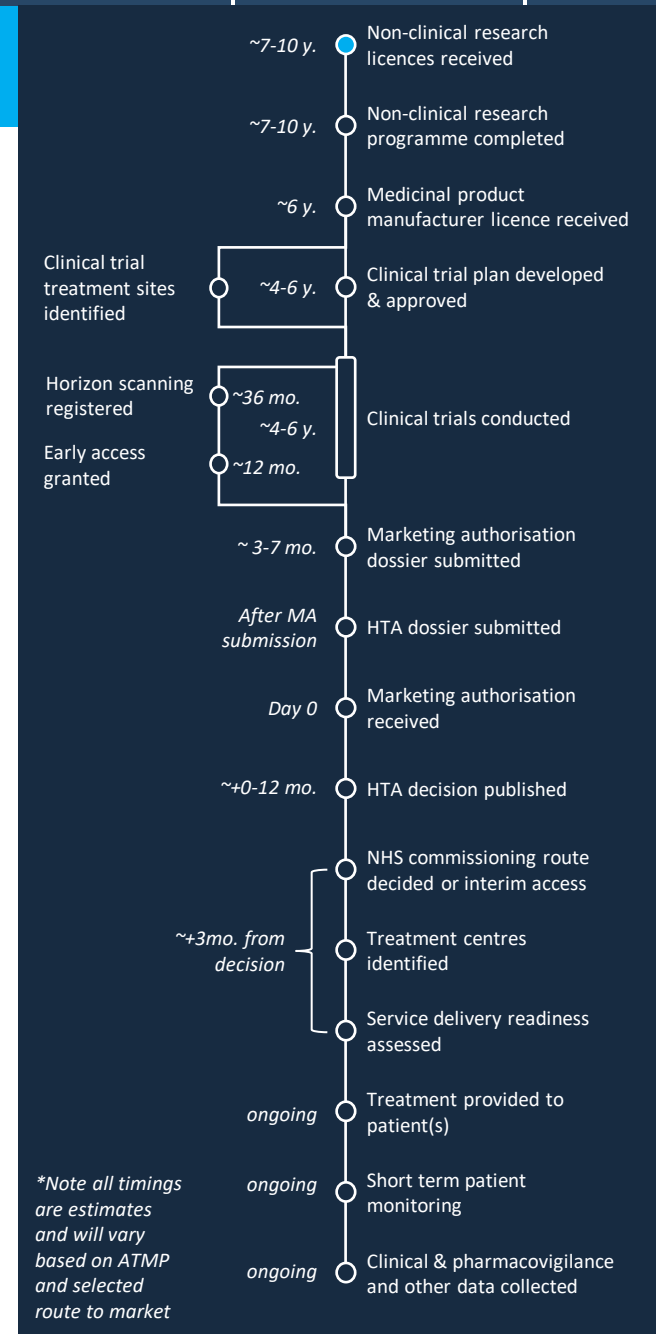
## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- ***In vitro* and *in vivo* studies**
- Delivery and diagnostic route assessment
- Research documentation consolidation

Overview | To-do list | **Output**

- *In vitro* study design, risk assessment, output and publication
- *In vivo* study design, risk assessment, output and publication
- Updated process documentation (including patent if applicable)

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- ***In vitro* and *in vivo* studies**
- Delivery and diagnostic route assessment
- Research documentation consolidation

## Overview

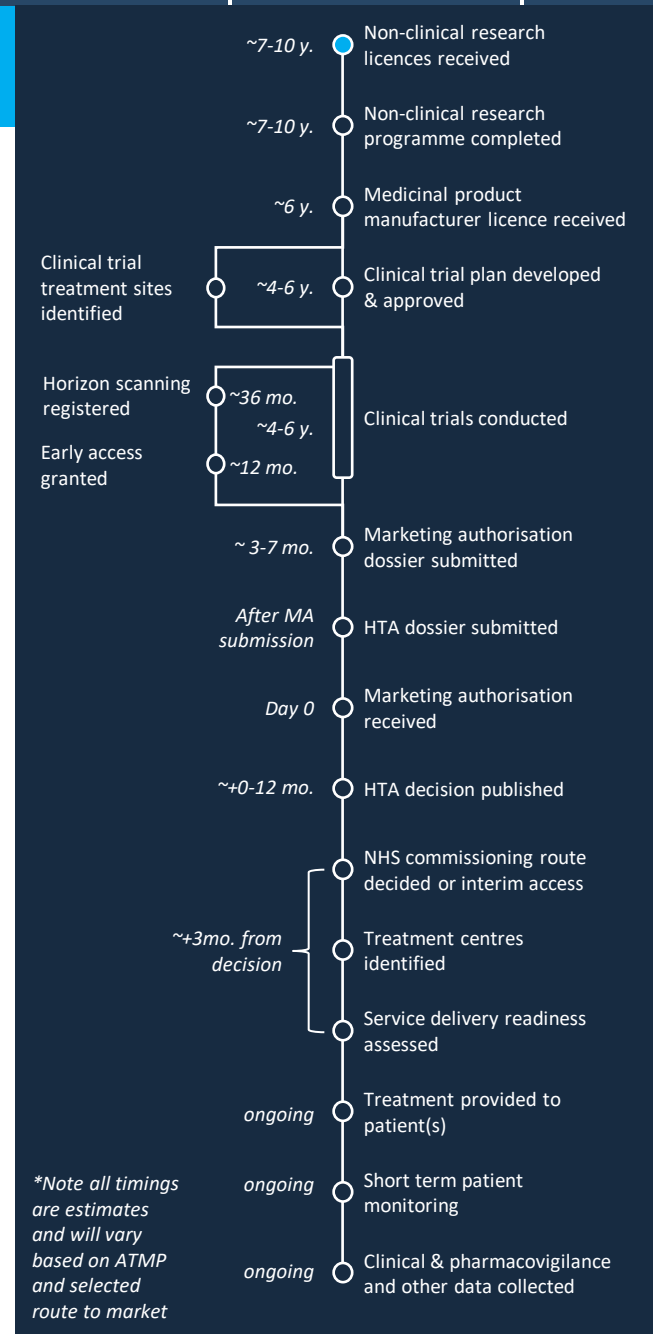
## To-do list

## Output

Regulatory and/or scientific advice

GxP compliance & certification

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

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- ***In vitro* and *in vivo* studies**
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- Research documentation consolidation

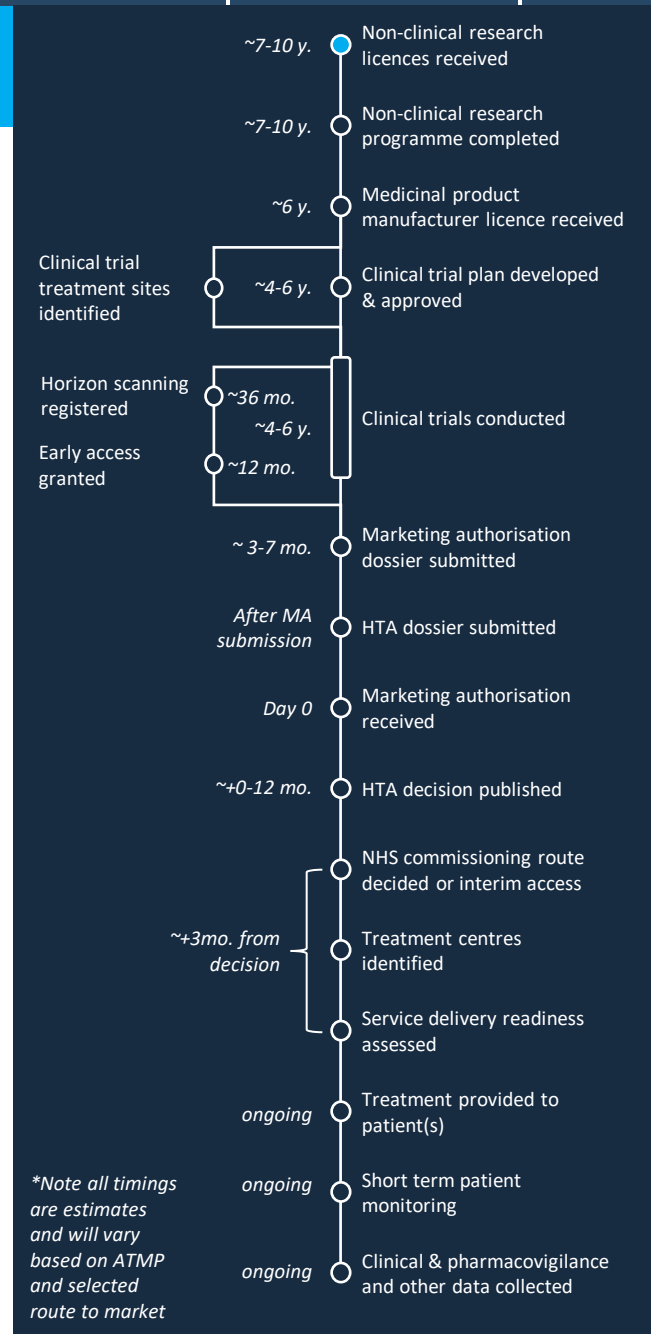
## Overview

## To-do list

## Output

- ATMP developer

**Linked steps** **Who is involved?** **Best practices & tips**



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- Manufacturing and supply chain planning
- ***In vitro* and *in vivo* studies**
- Delivery and diagnostic route assessment
- Research documentation consolidation

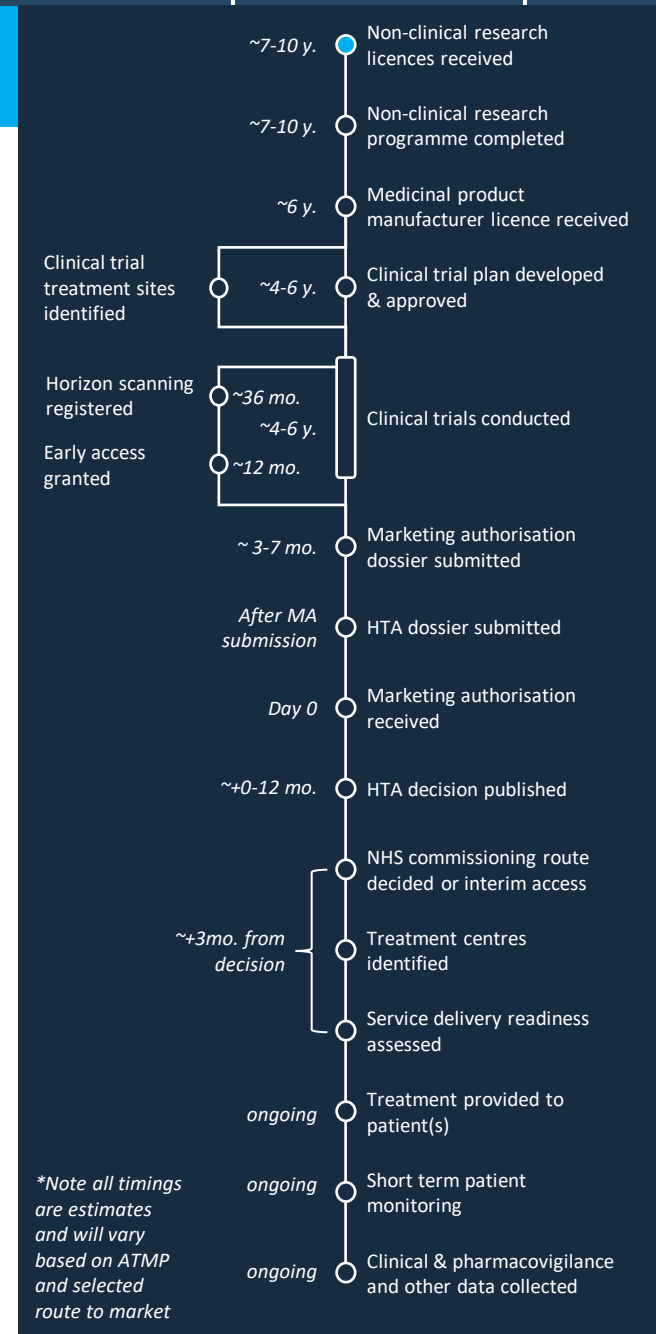
## Overview

## To-do list

## Output

- As part of non-clinical planning, it will be critical to have in place an ISO certified document management system to facilitate file management for regulatory approval steps
- Developers should be aware of any publication requirements as part of their funding and ensure that timelines are considered as peer-review can be time-consuming
- Developers are advised to consider how to involve patient groups in the development phase to ensure that the product targets the priorities of those it intends to treat

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- **Delivery and diagnostic route assessment**
- Research documentation consolidation

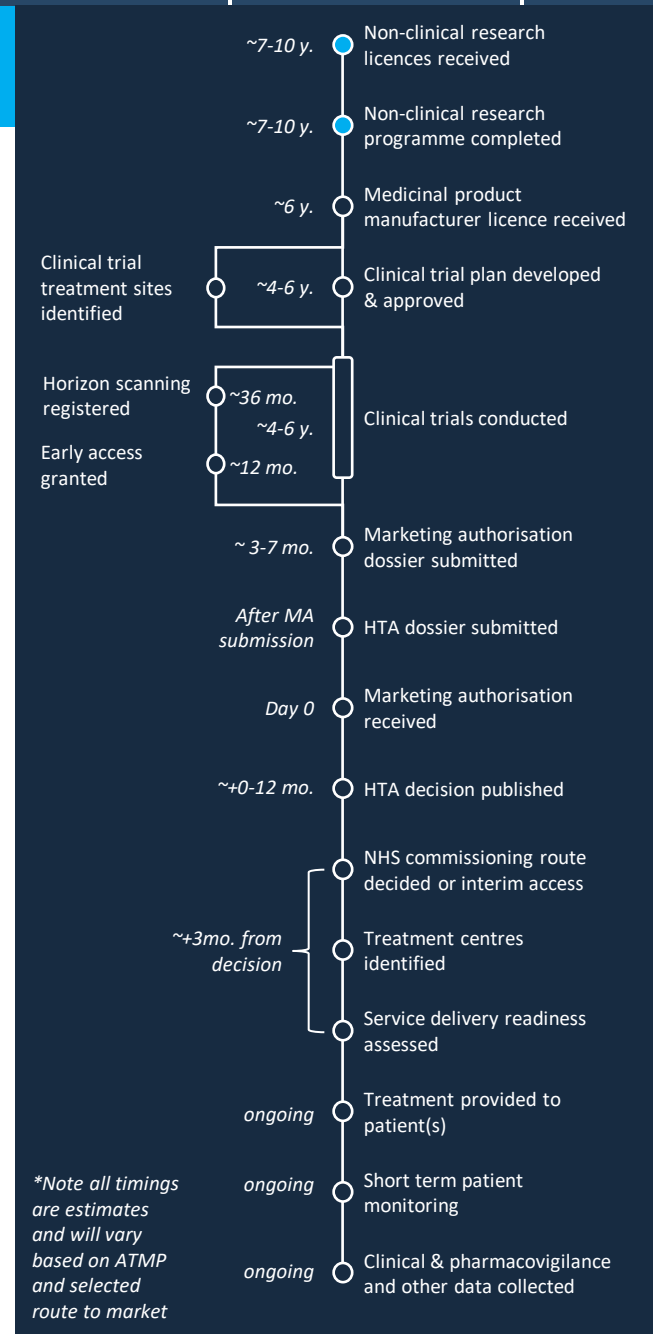
**Overview** | To-do list | Output

Developers should review the delivery method for their ATMP and assess the testing & diagnostic requirements during non-clinical research. If new diagnostic methods are required this should be highlighted early, and if new in vitro diagnostics are required, ensure to review the associated guidelines and processes.

Developers should review the patient journey for their intended product, identify any changes that may be required and ensure that these are considered as part of the overall research.

If new genomic tests are required, review the NHS Genomic Medicine Service (GMS) test directory and request an amendment for consideration during the GMS annual review

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- **Delivery and diagnostic route assessment**
- Research documentation consolidation

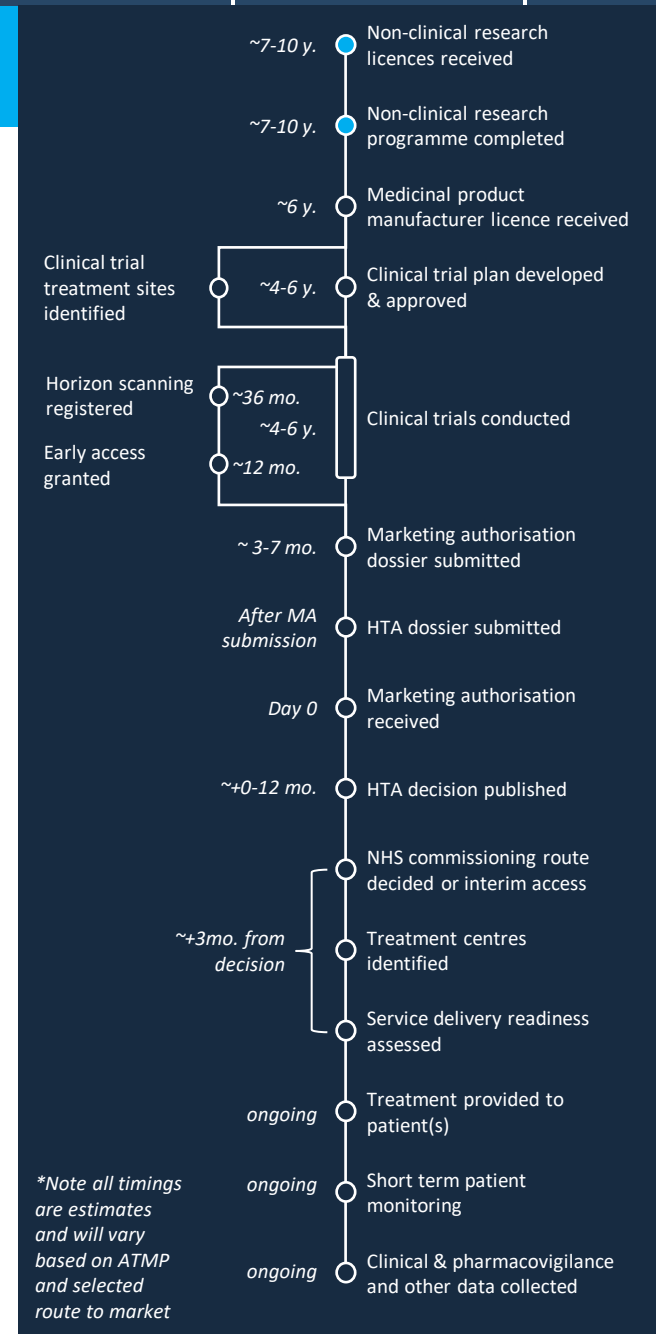
Overview | **To-do list** | Output

- Review ATMP delivery method
- Review ATMP patient journey and identify if changes may be required
- Review testing and diagnostic requirements within the patient journey
- Review guidance and requirements for regulating diagnostic devices
  - See Great Britain guidance here
  - See Northern Ireland guidance here
- Advise the Genomic Medicine Service of new genomic tests required here or email the Genomic Medicine Service at ENGLAND.testevaluation@nhs.net
- If including a medical device or diagnostic device component, review MHRA guidance on medical device and diagnostic regulation here

**When**

- During non-clinical research
- If advising Genomic Medicine Service, this should be done at least 6 months prior to expected commissioning

Linked steps | Who is involved? | Best practices & tips



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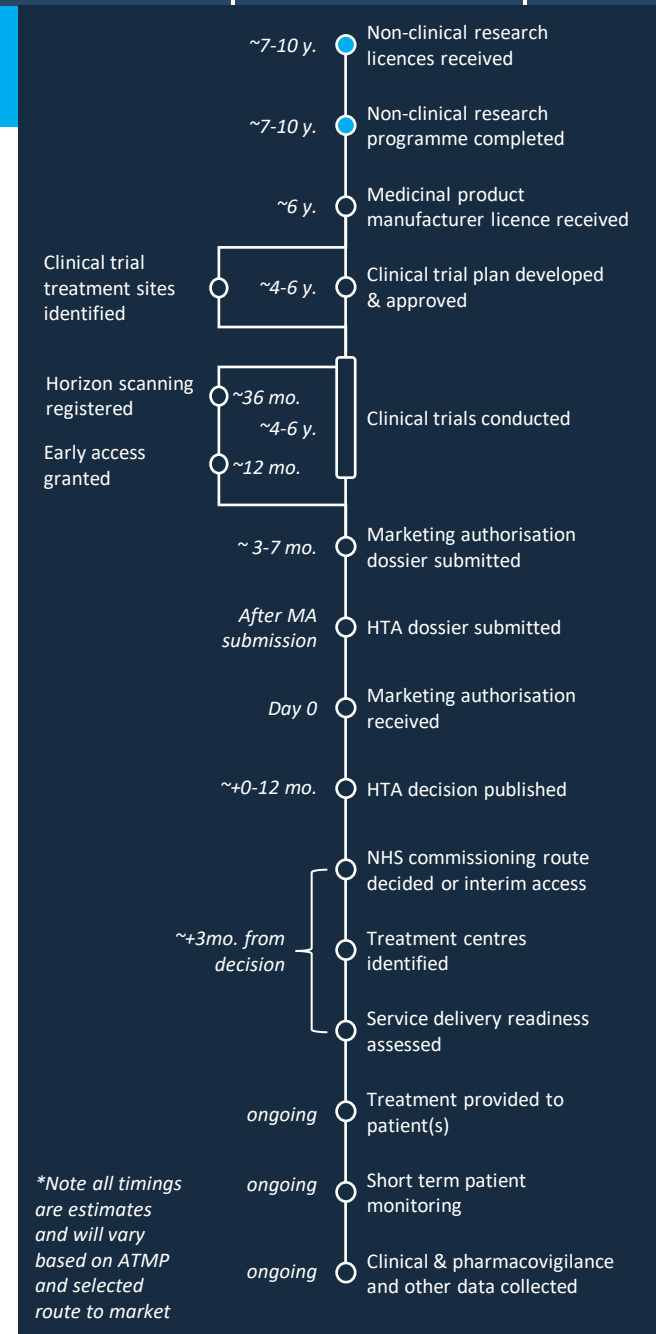
## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- **Delivery and diagnostic route assessment**
- Research documentation consolidation

Overview | To-do list | **Output**

- Review of product delivery method, testing and diagnostic requirements
- Advise relevant stakeholders of any new tests required




Linked steps | Who is involved? | Best practices & tips

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- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- **Delivery and diagnostic route assessment**
- Research documentation consolidation

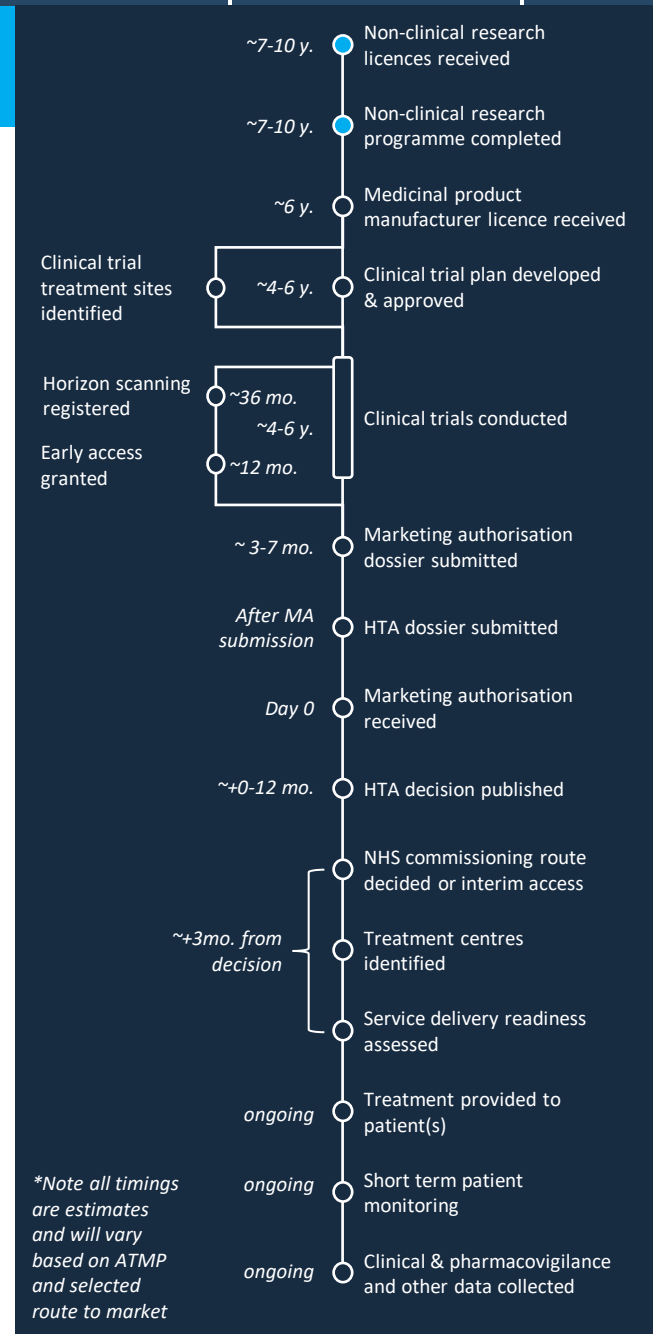
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- **Delivery and diagnostic route assessment**
- Research documentation consolidation

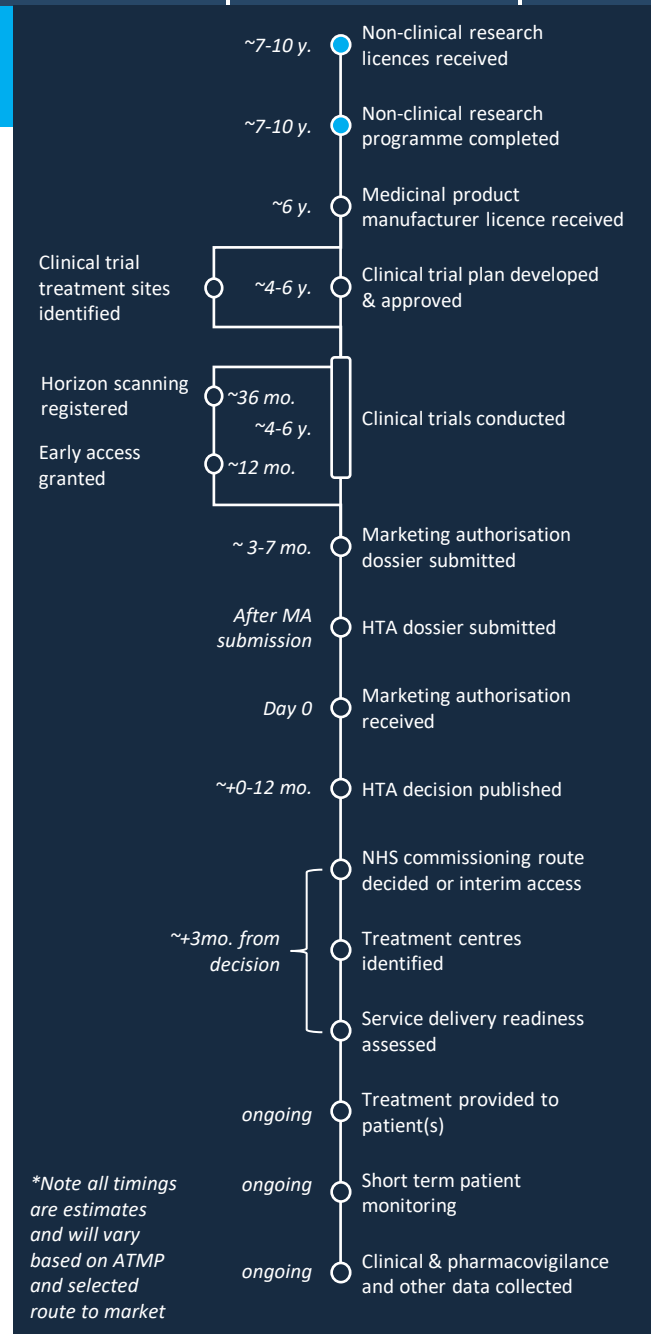
## Overview

- ATMP developer

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- Animal model identification & sourcing
- Manufacturing and supply chain planning
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- **Delivery and diagnostic route assessment**
- Research documentation consolidation

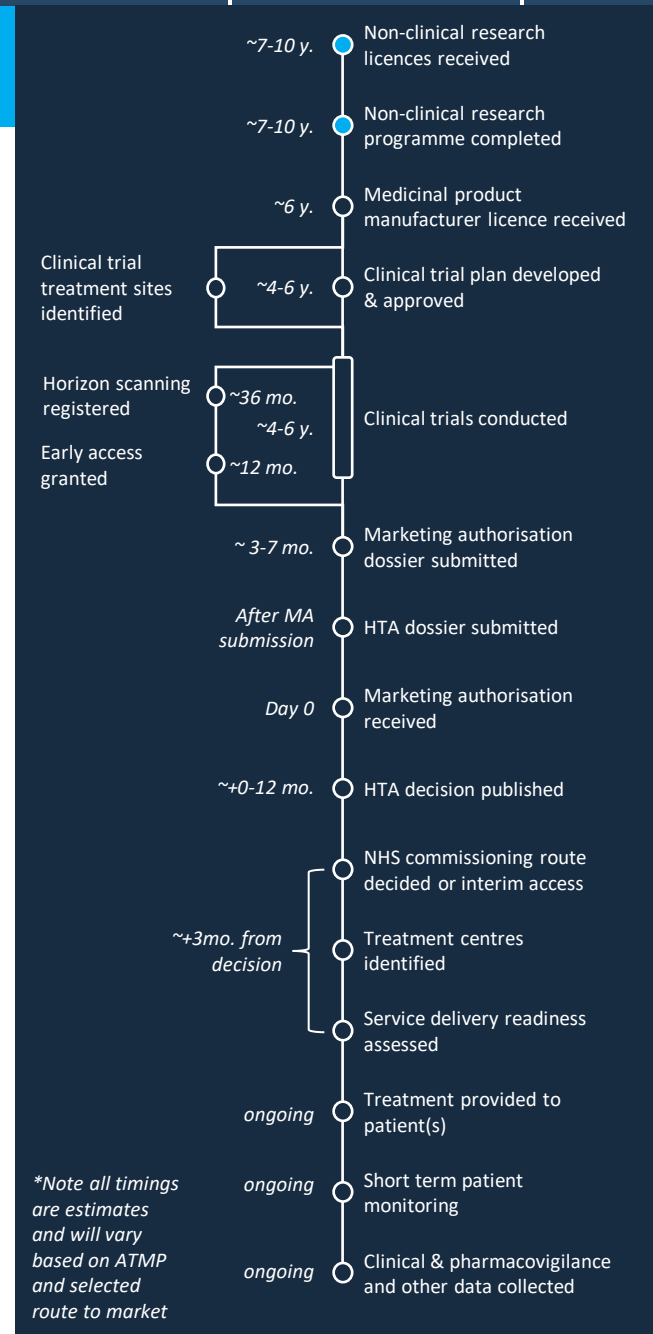
## Overview

## To-do list

## Output

- When reviewing the patient journey and diagnostic pathways, developers are advised to consider consulting patient groups and use of patient and public involvement (PPI), links to useful guidance from National Institute for Health Research (NIHR) can be found here

**Linked steps** **Who is involved?** **Best practices & tips**



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- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- **Research documentation consolidation**

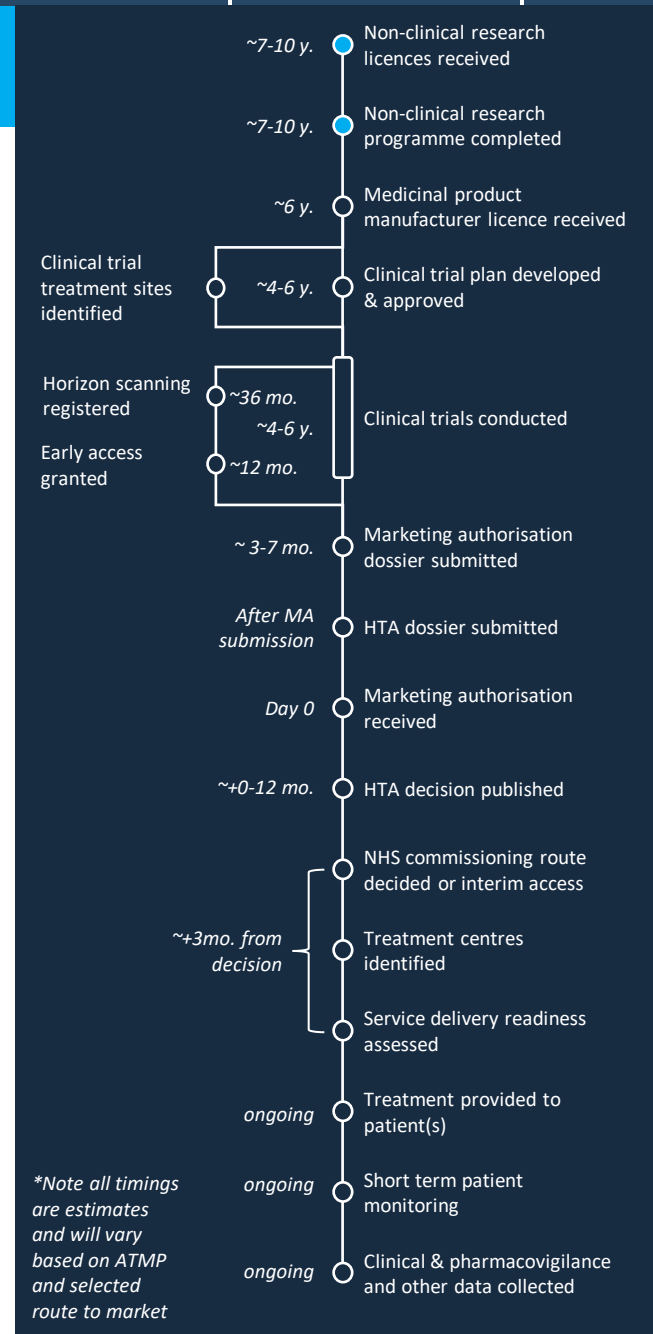
**Overview** | To-do list | Output

Prior to clinical trial application, ATMP developers should review the guidance documentation for conducting clinical trials in the UK and consolidate non-clinical research documentation in preparation for their clinical trial application.

After receipt of clinical trial authorisation, ATMP developers must ensure that all of their Trial Management documentation (including documentation of approvals/authorisations) has been obtained and is version controlled.

Developers may also complete a trial document checklist to ensure that all documentation is in place.

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- **Research documentation consolidation**

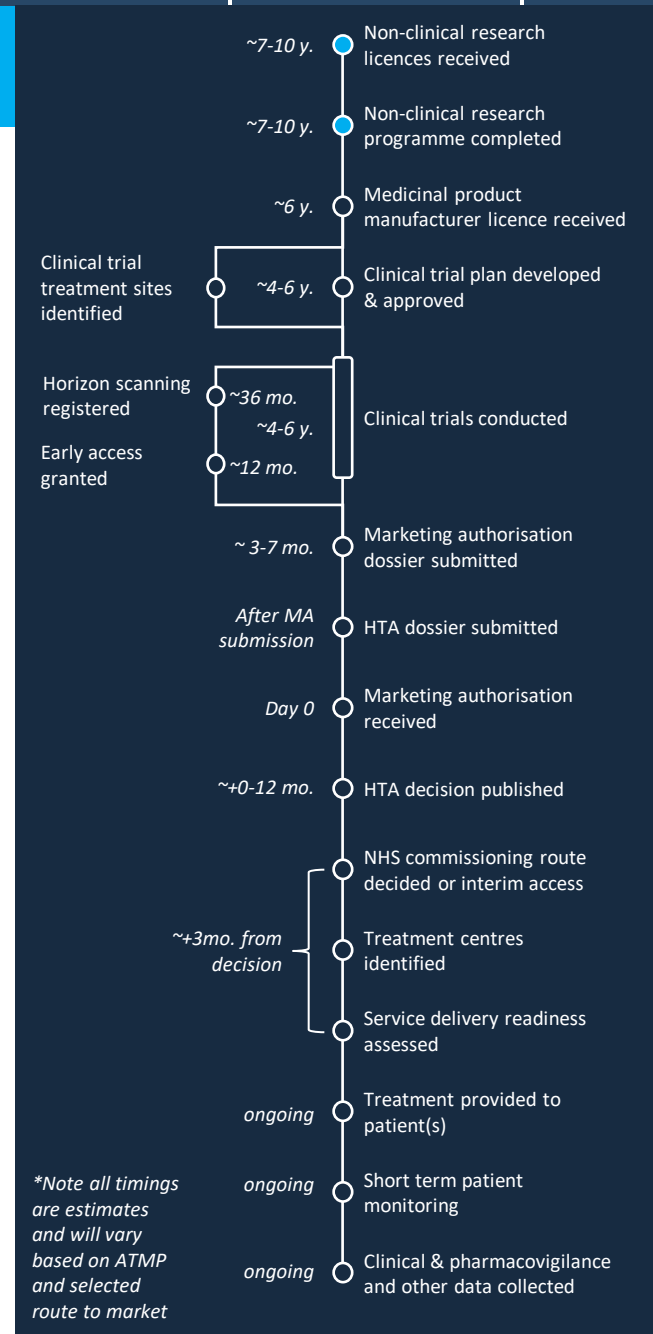
Overview | **To-do list** | Output

- General guidance on documentation required for clinical trial applications can be found here
- Further guidance including a trial document checklist can be found here

**When**

- Consolidation prior to submission of clinical trial application
- Trial management documentation checklist and ongoing management upon receipt of clinical trial authorisation

**Linked steps** | **Who is involved?** | **Best practices & tips**



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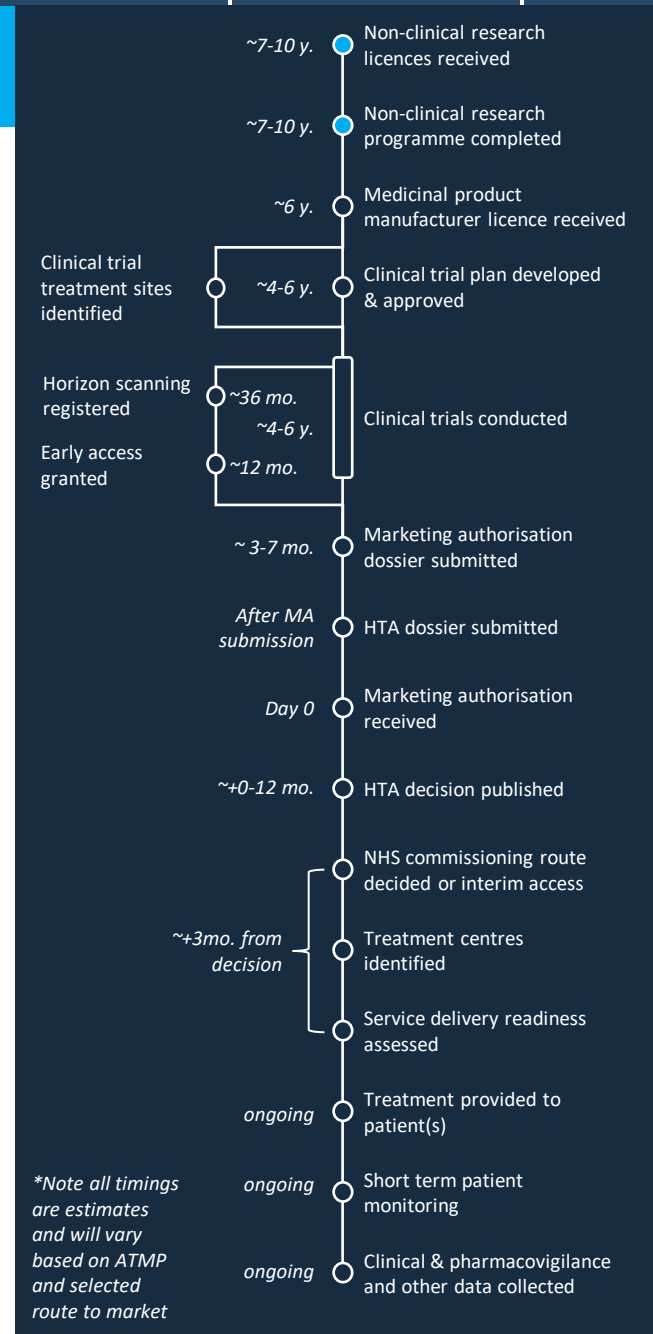
## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- **Research documentation consolidation**

Overview | To-do list | **Output**

- Trial management documentation obtained and confirmed

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- Animal model identification & sourcing
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- **Research documentation consolidation**

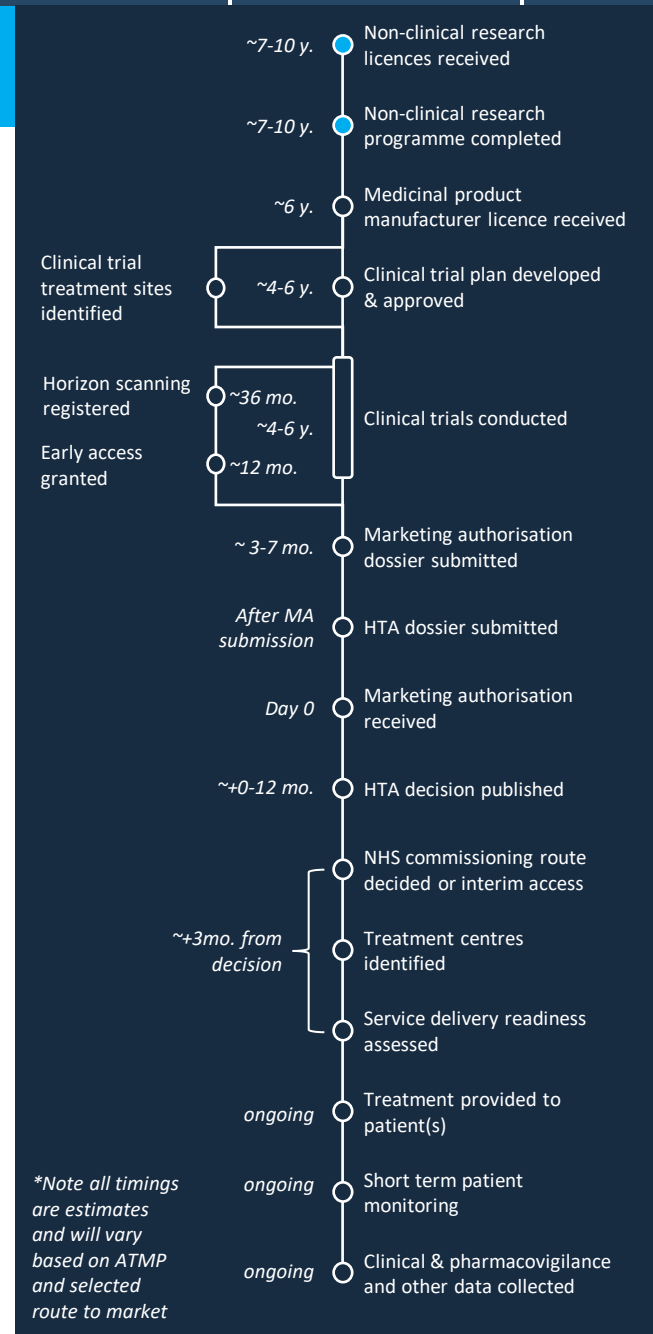
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- Animal model identification & sourcing
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- Delivery and diagnostic route assessment
- **Research documentation consolidation**

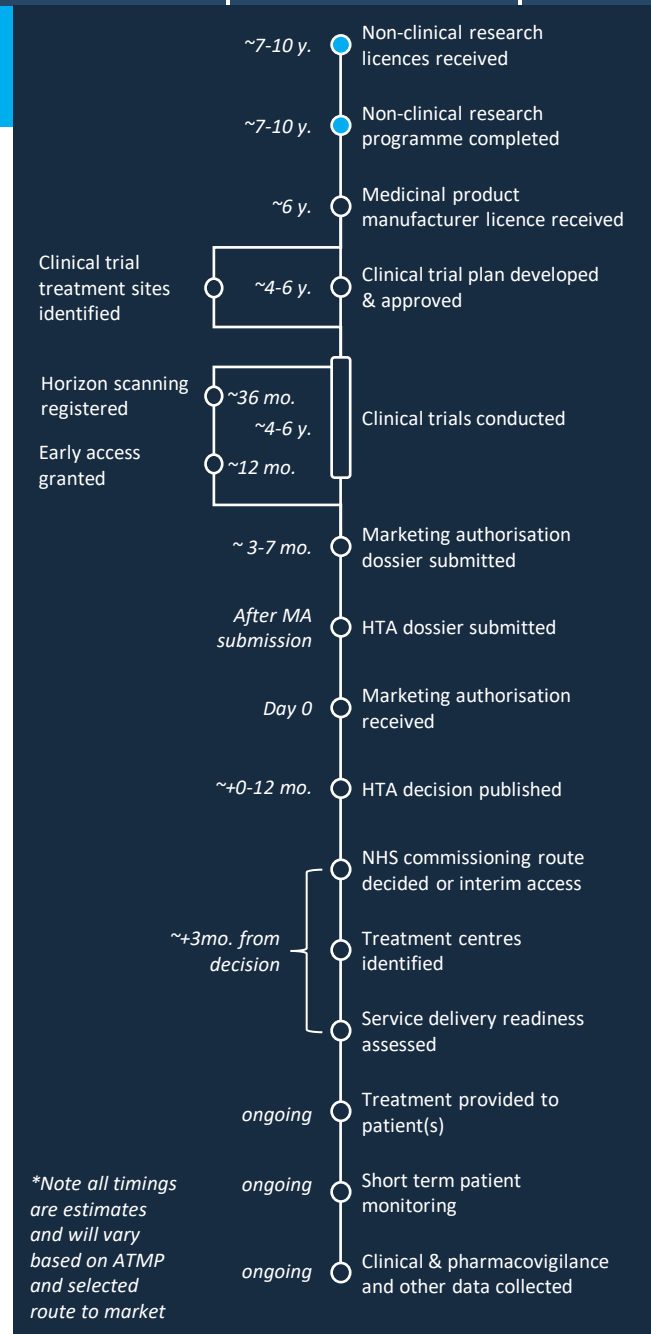
Overview

- ATMP developer

To-do list

Output

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Animal model identification & sourcing
- Manufacturing and supply chain planning
- *In vitro* and *in vivo* studies
- Delivery and diagnostic route assessment
- **Research documentation consolidation**

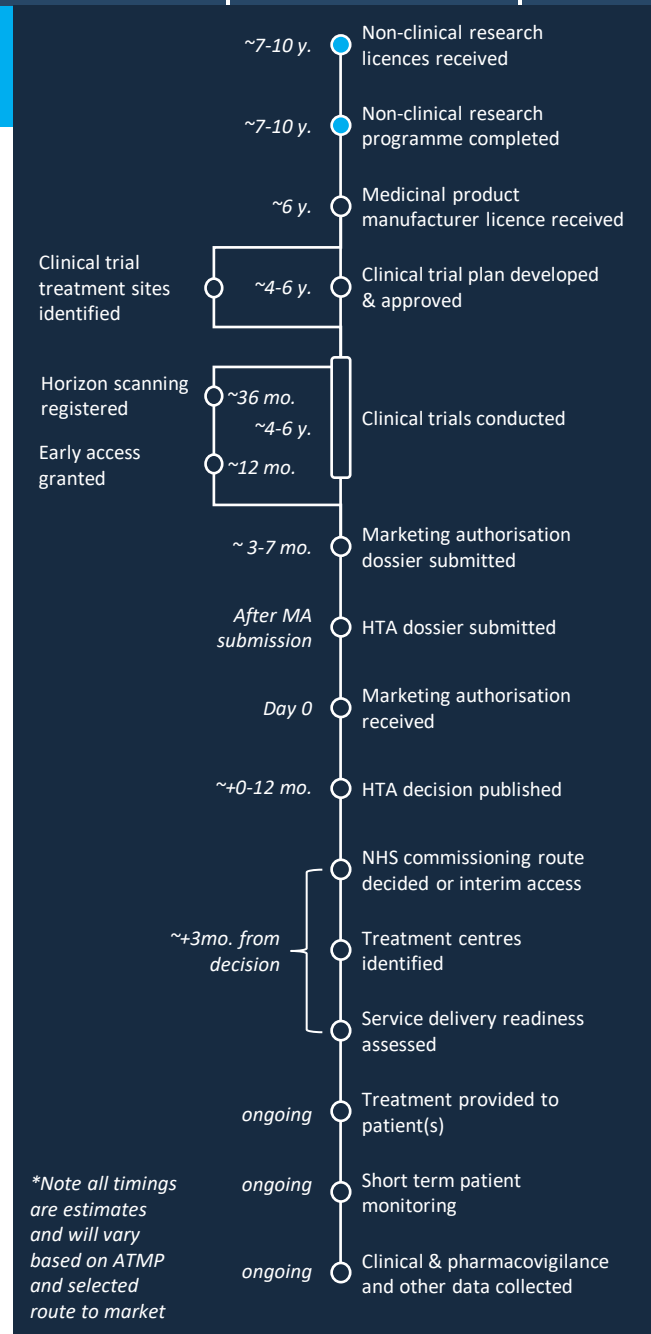
## Overview

## To-do list

- Ensure that ISO certified document management system is in place for technical files to facilitate file management for clinical trial application and later regulatory approval steps

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What licences and/or approvals are required to conduct research?**

2 What key regulatory steps are required to receive marketing authorisation?

3 What programmes are available to accelerate time to market?

## KEY TOPICS

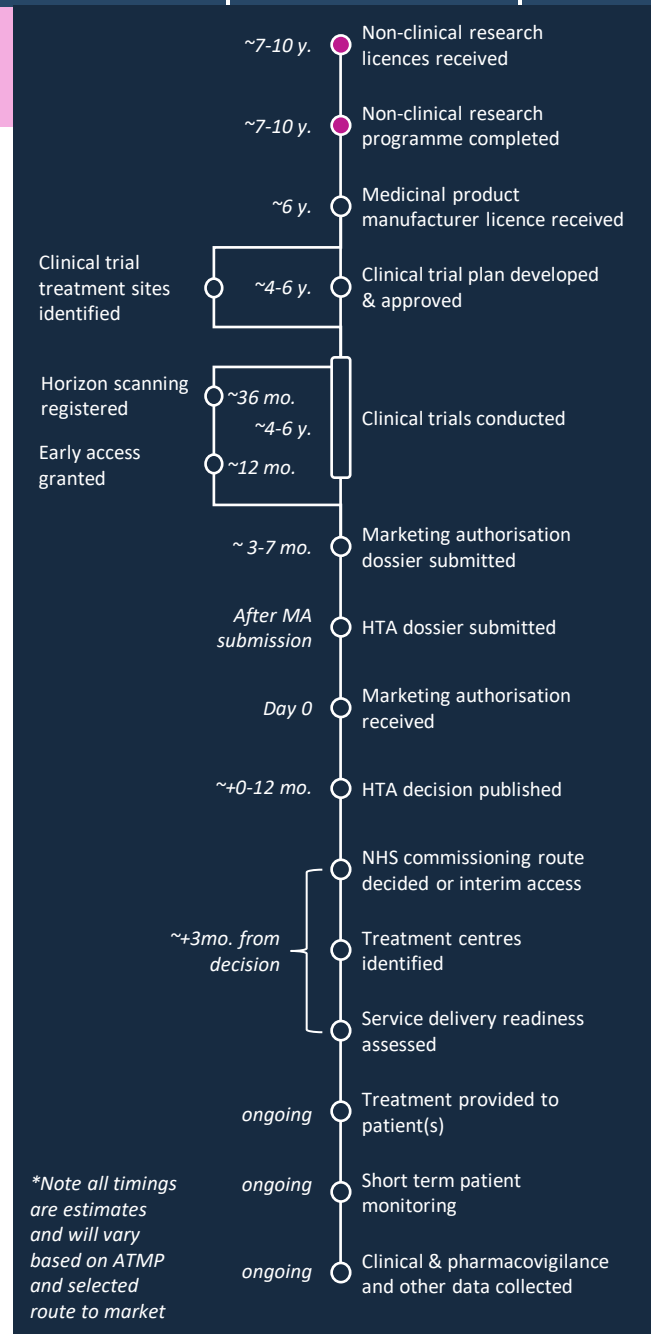
- **Genetically Modified Organisms notification [if applicable]**
- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

**Overview** | To-do list | Output

For developers using any Genetically Modified Organisms (GMO) in research or as part of the ATMP development process (for both on premises and contained use), consult and review the Health and Safety Executive (HSE) guidelines to determine if notification of the HSE is required.

If the ATMP or research type is identified as meeting the criteria of use of GMOs, developers must notify the HSE. Any clinical sites where GMOs are being used or stored must also notify the HSE. There are fees involved for HSE notifications.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



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## KEY TOPICS

- **Genetically Modified Organisms notification [if applicable]**
- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

Overview | **To-do list** | Output

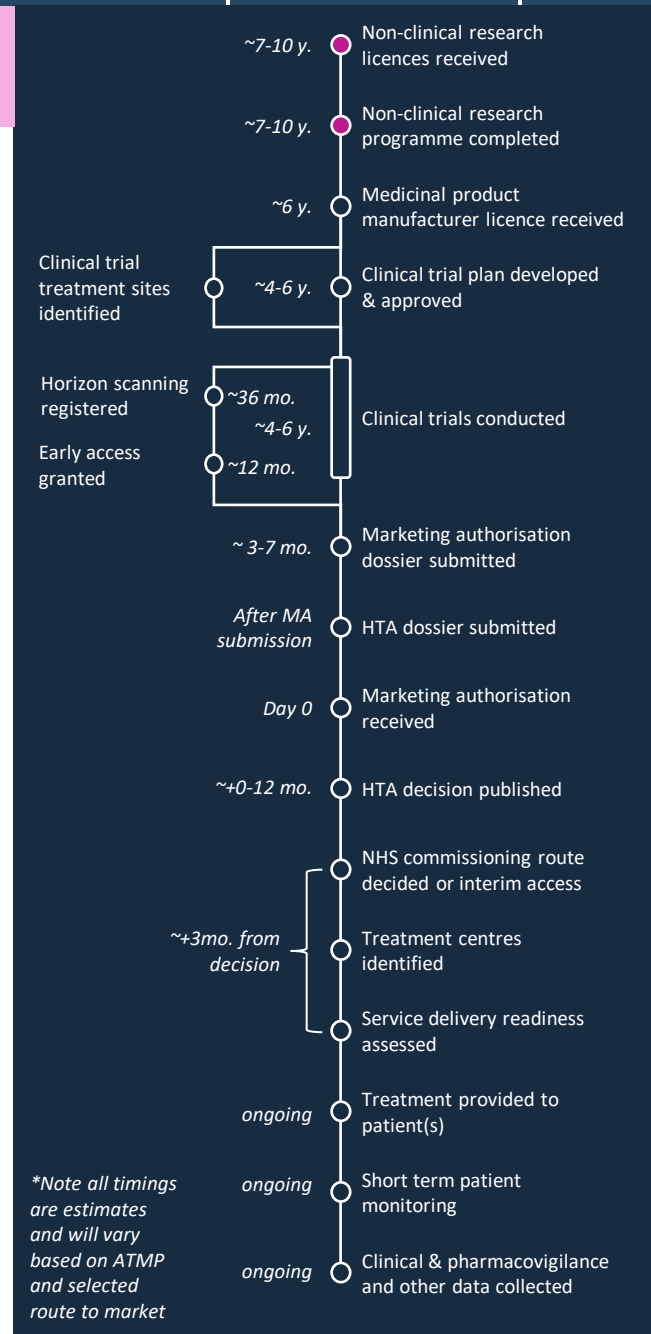
- Review HSE guidelines on the use of Genetically Modified Organisms here
- If required for the ATMP type, notify the HSE using their online form here

**When**

Before commencing non-clinical research

Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**



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## KEY TOPICS

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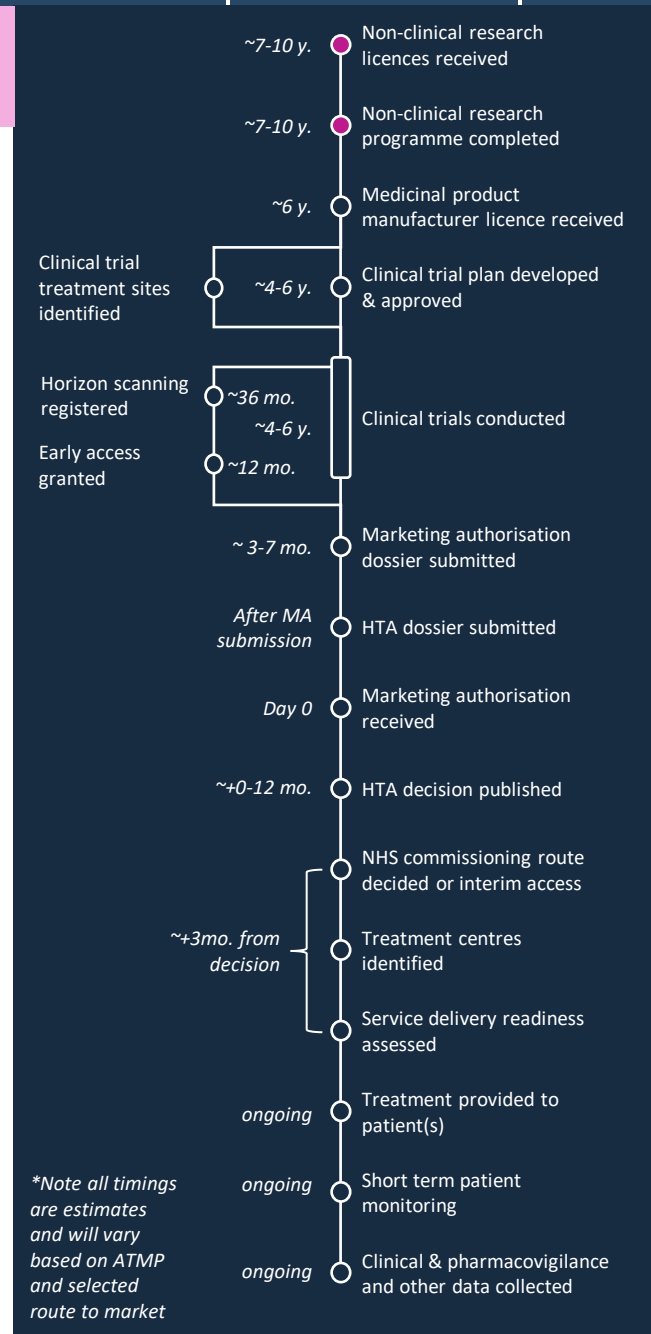
- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

Overview | To-do list | **Output**

- Notification of use of GMOs to the HSE

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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## KEY TOPICS

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- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

Overview

To-do list

Output

Service delivery readiness

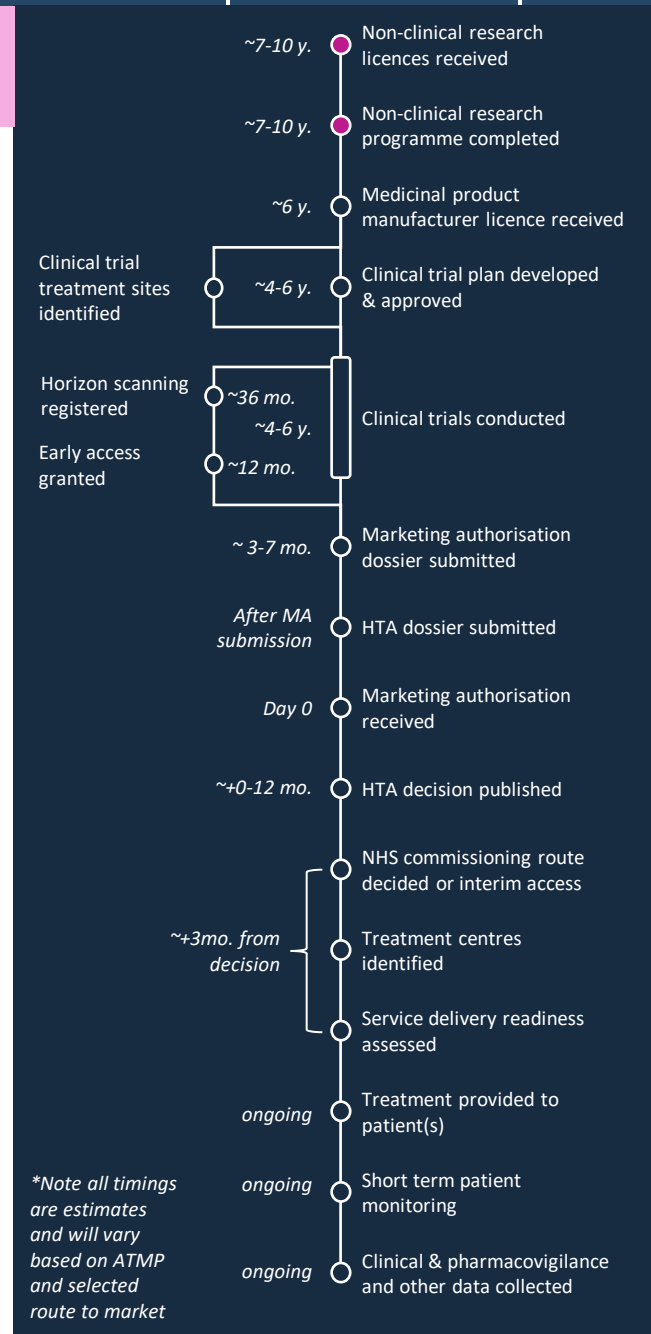
Regulatory and/or scientific advice

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



**1 What licences and/or approvals are required to conduct research?**

2 What key regulatory steps are required to receive marketing authorisation?

3 What programmes are available to accelerate time to market?

## KEY TOPICS

- **Genetically Modified Organisms notification [if applicable]**
- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

Overview

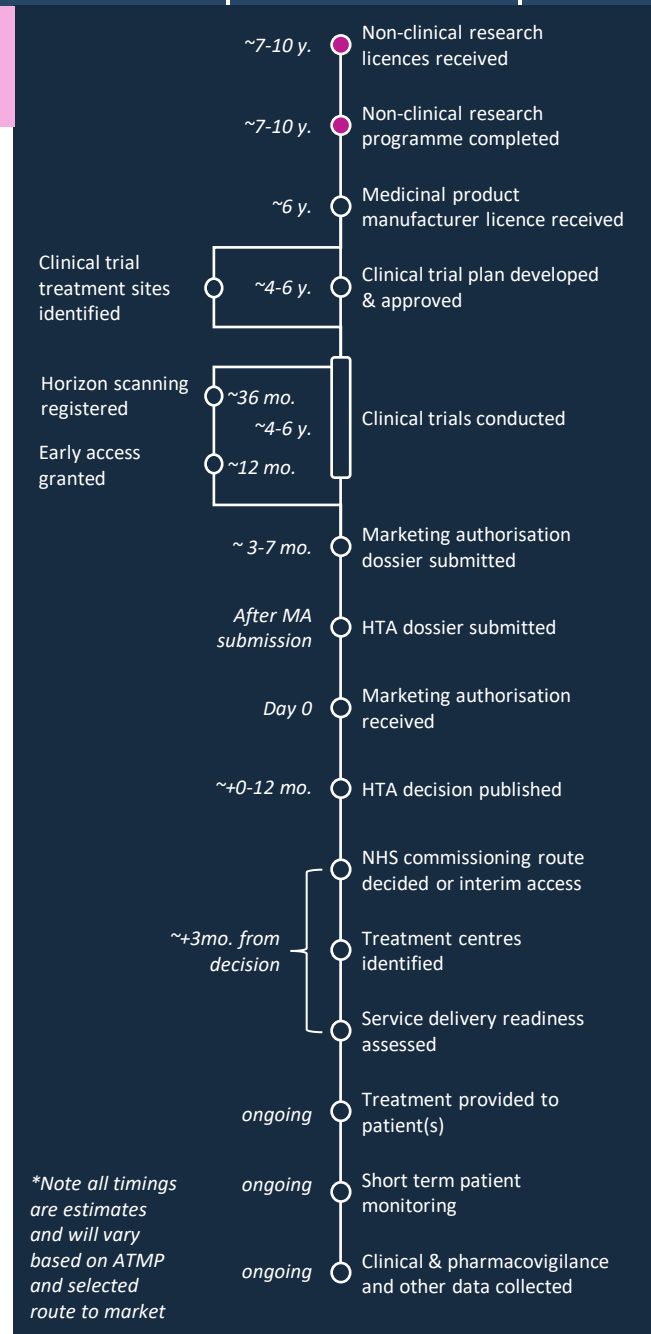
To-do list

Output

- ATMP developer
- Health and Safety Executive (HSE)
- Clinical site

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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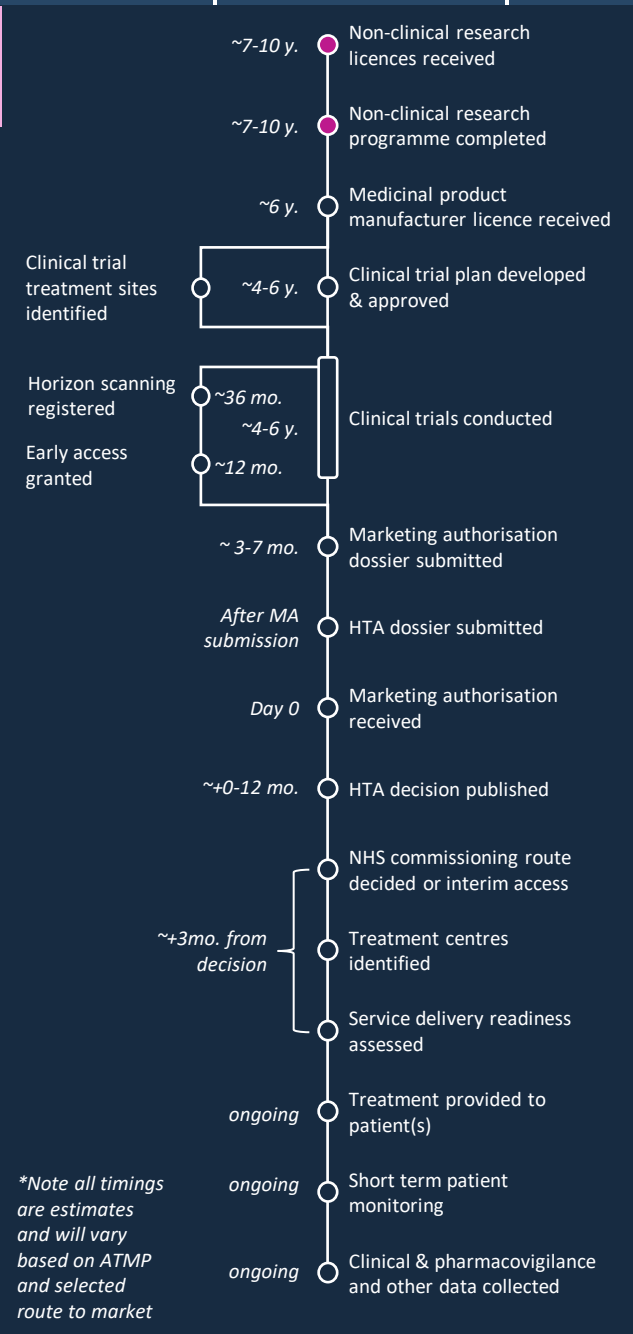
- UKCA marking coordination [if applicable]

Overview | To-do list | Output

- You can get advice on administrative matters relating to the submission of notifications under the Genetically Modified Organisms (Contained Use) Regulations by contacting the HSE Notifications Officer on bioagents@hse.gov.uk




Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype

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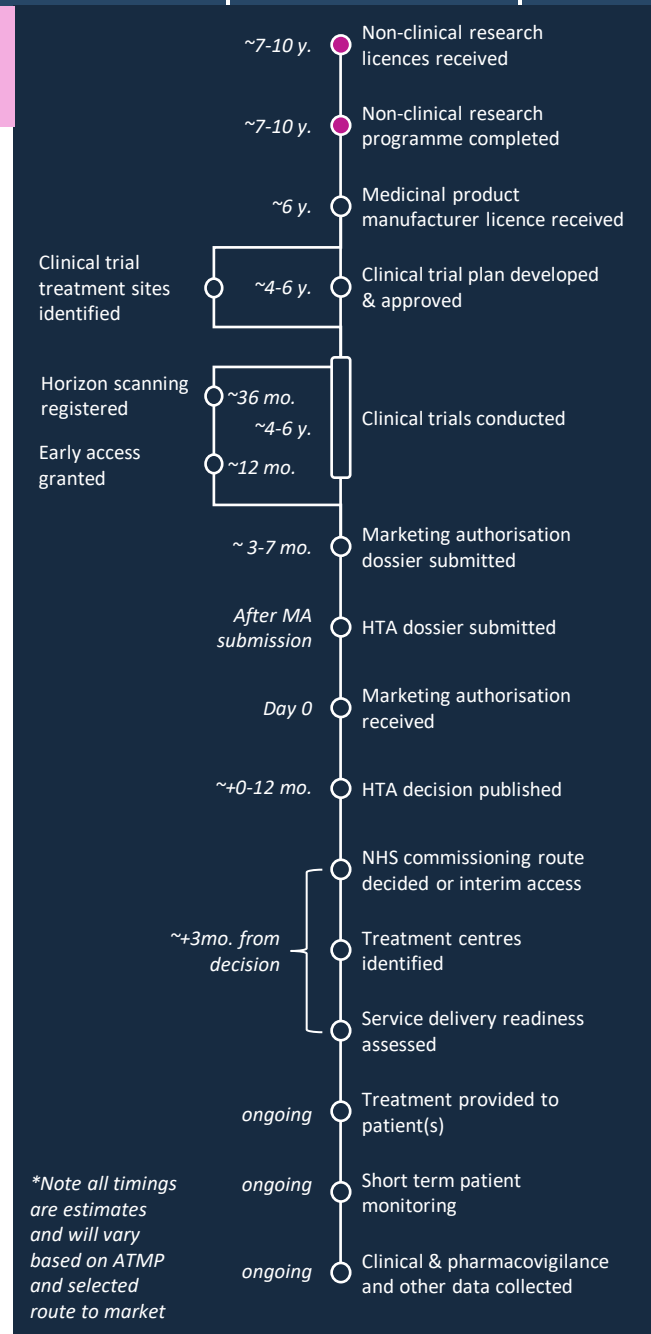
**Overview** | To-do list | Output

If tissues and cells are being used as starting materials in a medicinal product, the donation, procurement and testing of the cells are covered by the Tissues and Cells Directive (2004/23/EC) and may require a licence from the Human Tissue Authority (HTA).

Review HTA guidance on procurement, testing and licensing of human cells/tissue use and submit a licence application (if required). There are fees associated with HTA licensing. If materials are being processed, manufactured or sourced from outside the UK, there may be national guidelines in place regarding import and export licensing requirements (in addition to those required by the HTA).

Note: some gene therapies (i.e. *ex-vivo*) still require HTA licensing




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

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## KEY TOPICS

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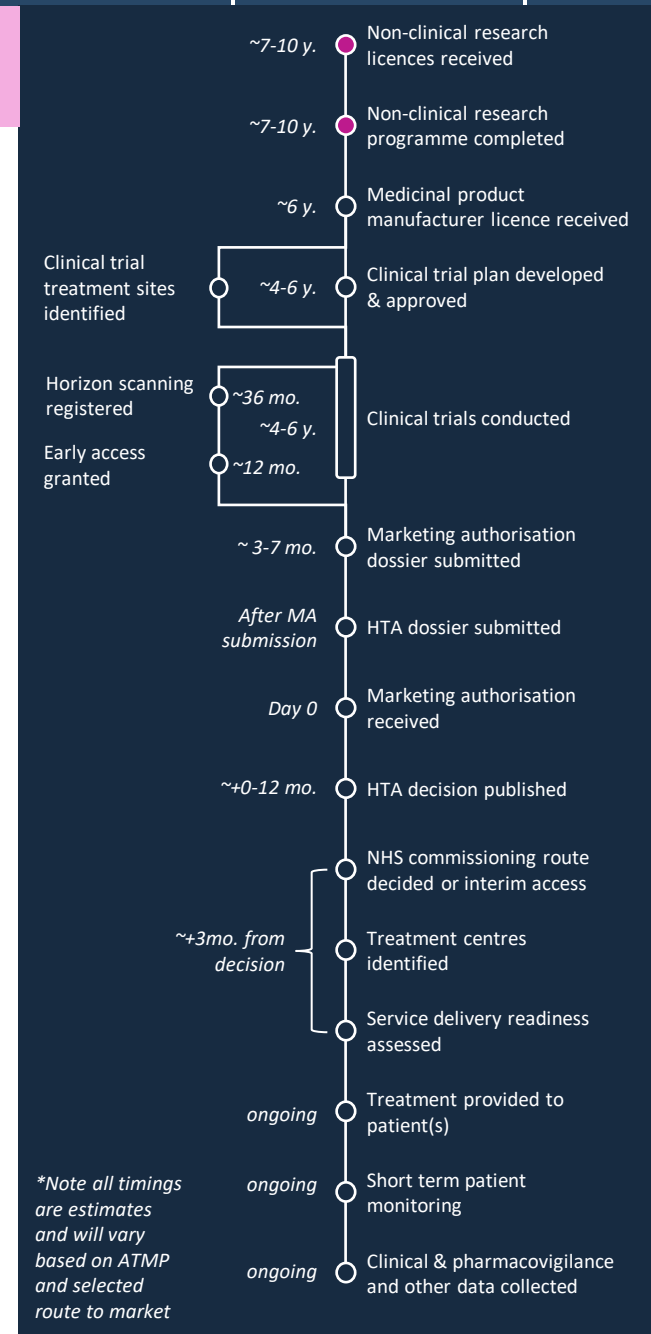
- UKCA marking coordination [if applicable]

Overview | **To-do list** | Output

- Review HTA guidance on licensing of human cells/tissues and determine if a licence is required here
- Review the steps you need to take before applying for a licence (if required) here
- Note: licensing requirements for import/export to the EEA are different for establishments in Northern Ireland than for the rest of Great Britain
- Review import/export licensing requirements and guidance
  - For establishments in Great Britain see guidance here
  - For establishments in Northern Ireland see guidance here
- To apply for an HTA licence access the licence forms here
- Review any relevant guidelines relating to the country of origin/processing/manufacture of ATMP components to ensure compliance and apply for any relevant licences

**When**

Before commencing non-clinical research




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

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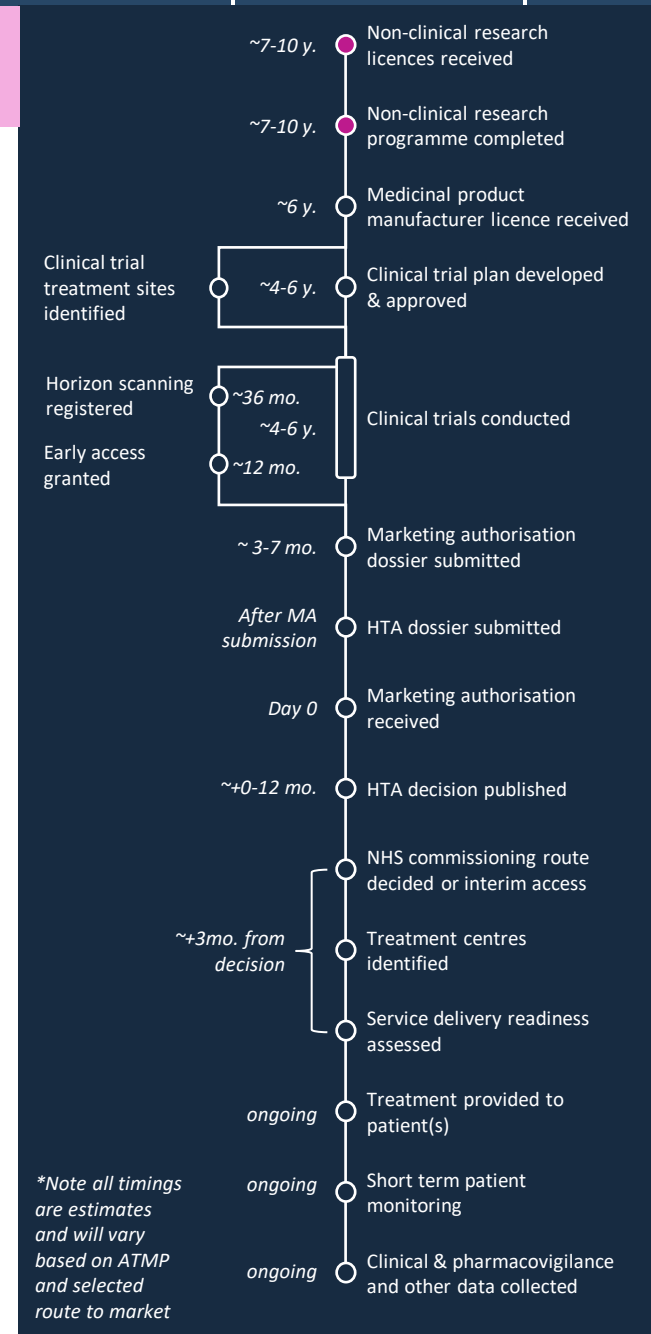
Overview | To-do list | **Output**

- HTA licence types required for the ATMP identified and guidance reviewed
- HTA licence application(s) submitted
- Receipt of requisite HTA licence




Linked steps | Who is involved? | Best practices & tips

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Overview

To-do list

Output

Service delivery readiness

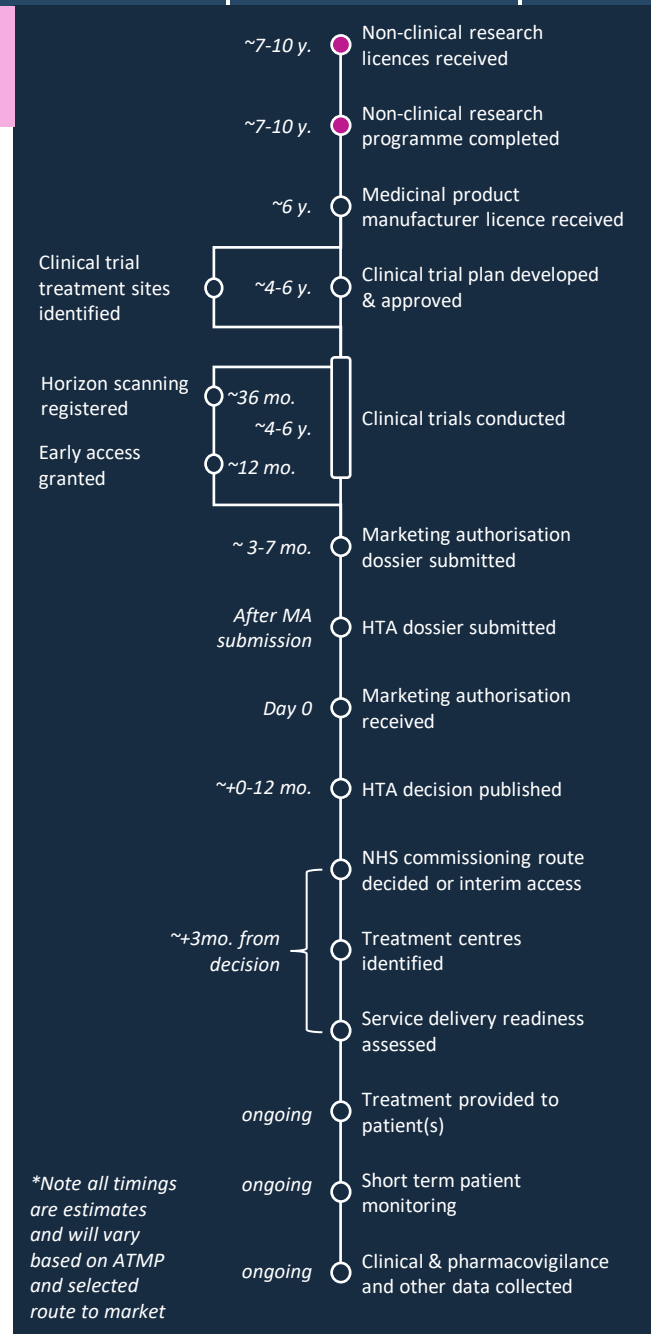
Regulatory and/or scientific advice

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



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- UKCA marking coordination [if applicable]

## Overview

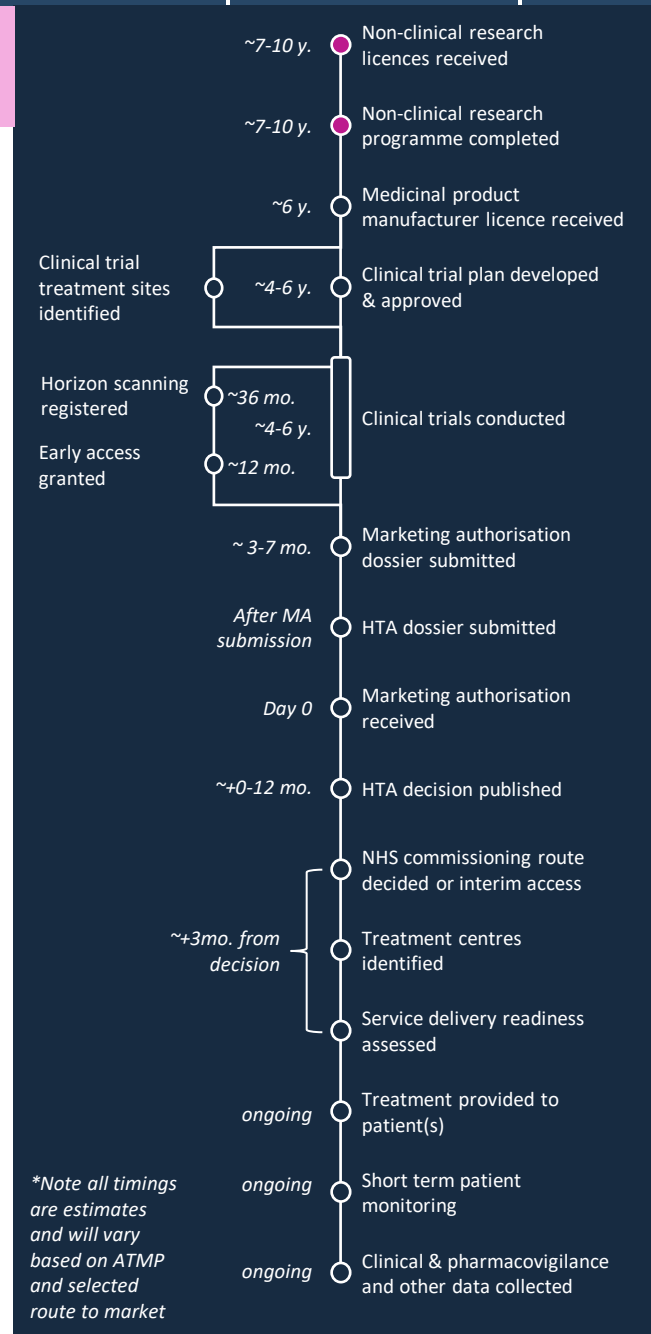
## To-do list

## Output

- ATMP developer
- Human Tissue Authority (HTA)

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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## Overview

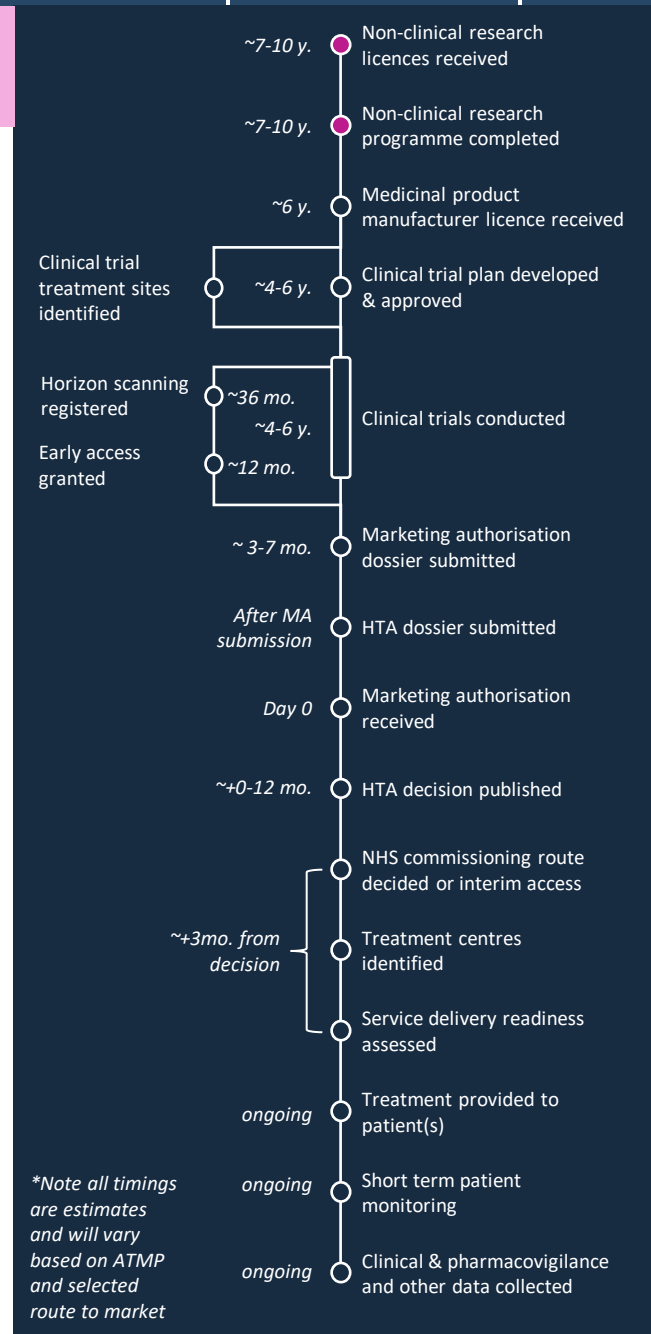
## To-do list

## Output

- If you have any queries, review the FAQs here or contact the HTA at licensing.enquiries@hta.gov.uk

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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**Overview** | To-do list | Output

Good Practice (GxP) should be central to the development of all ATMPs, including Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Pharmacovigilance Practice (GPvP) and if applicable, Good Distribution Practice (GDP).

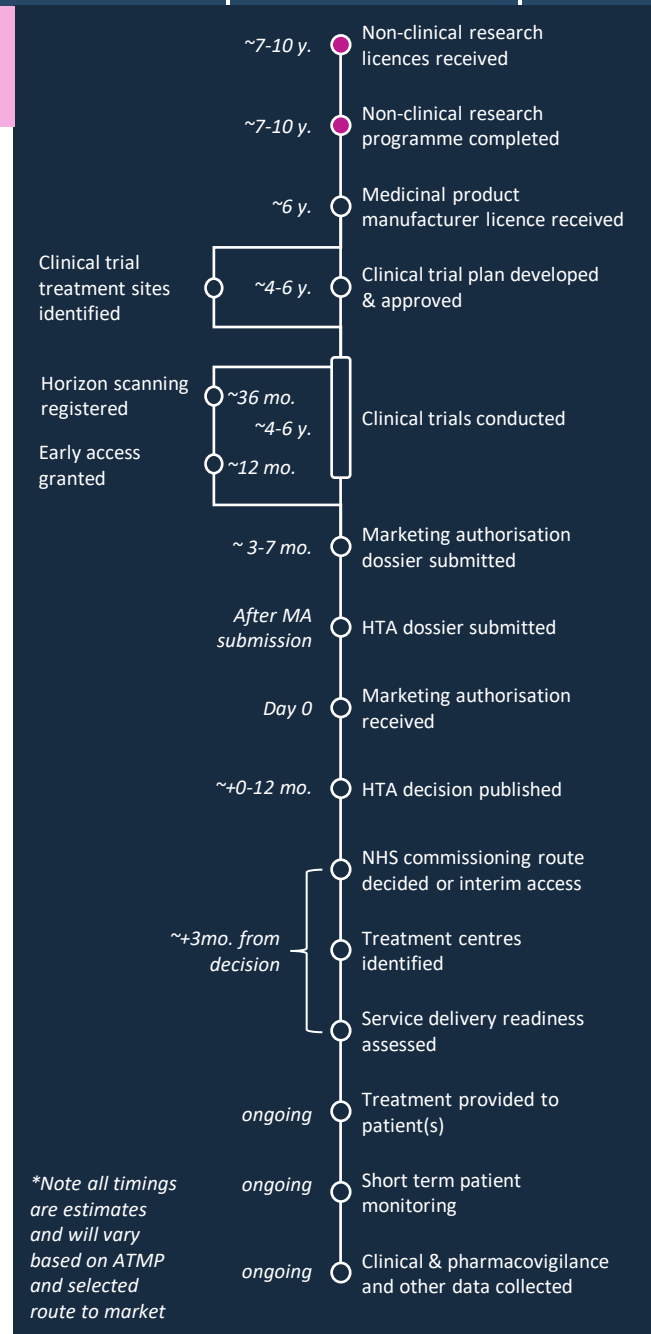
Developers should review guidelines and resources from the EMA* on Good Manufacturing Practice (GMP) in relation to ATMPs to ensure compliance throughout the development and manufacturing phase, or if outsourcing, engage with identified GMP manufacturer.

The EMA has published GLP and GCP principles in relation to ATMPs to aid non-clinical study preparation. The MHRA also requires certification, inspection and membership of the UK GLP compliance monitoring programme run by the UK GLP Monitoring Authority (UK GLPMA). The programme is only open to facilities in the UK and requires a membership fee.

When planning clinical trials, compliance with Good Clinical Practice (GCP) requirements must be met and included in the trial design, this includes requirements for trial management, reporting and documentation.

*EMA ATMP specific guidelines are still recommended as a useful source of guidance post-brexit transition

Linked steps | Who is involved? | Best practices & tips



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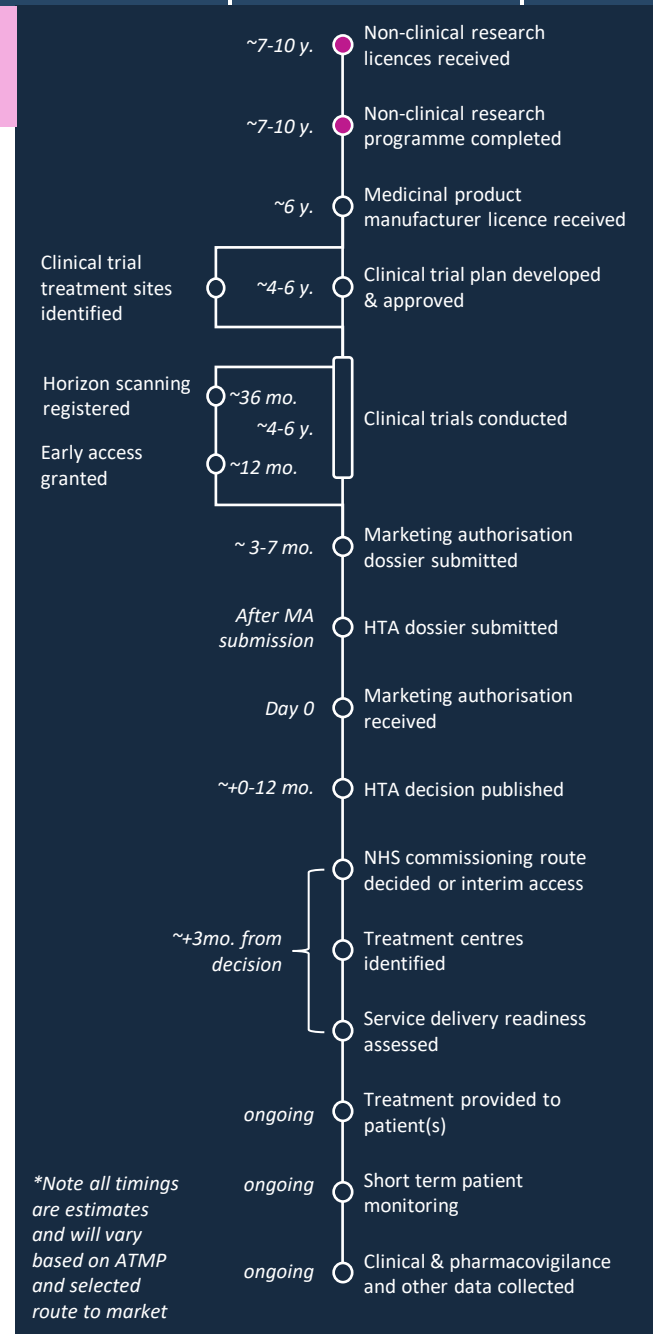
Overview | **To-do list** | Output

- Review guidelines and resources from the EMA on GMP in relation to ATMPs here
  - If outsourcing, engage with the identified manufacturer to ensure compliance with GMP
- Review GLP principles in relation to ATMPs here
- Review Q&A on use of materials of biological origin here
- Review UK-specific GLP guidance from the MHRA here
- Apply to the GLP compliance monitoring programme through the application form here
- Review EMA guidance on GCP guidelines and requirements for ATMPs here
- Review EMA ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) GCP guidelines here
- Review general guidance for preparing for conducting clinical trials in the UK here
- EMA guidance on Good Pharmacovigilance Practices (GPvP) can be found here with MHRA guidance on their application in the UK here
- Review MHRA guidance on Good Distribution Practice (GDP) here

**When**

GMP and GLP requirements should be met before commencing non-clinical research

**Linked steps** | **Who is involved?** | **Best practices & tips**



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## KEY TOPICS

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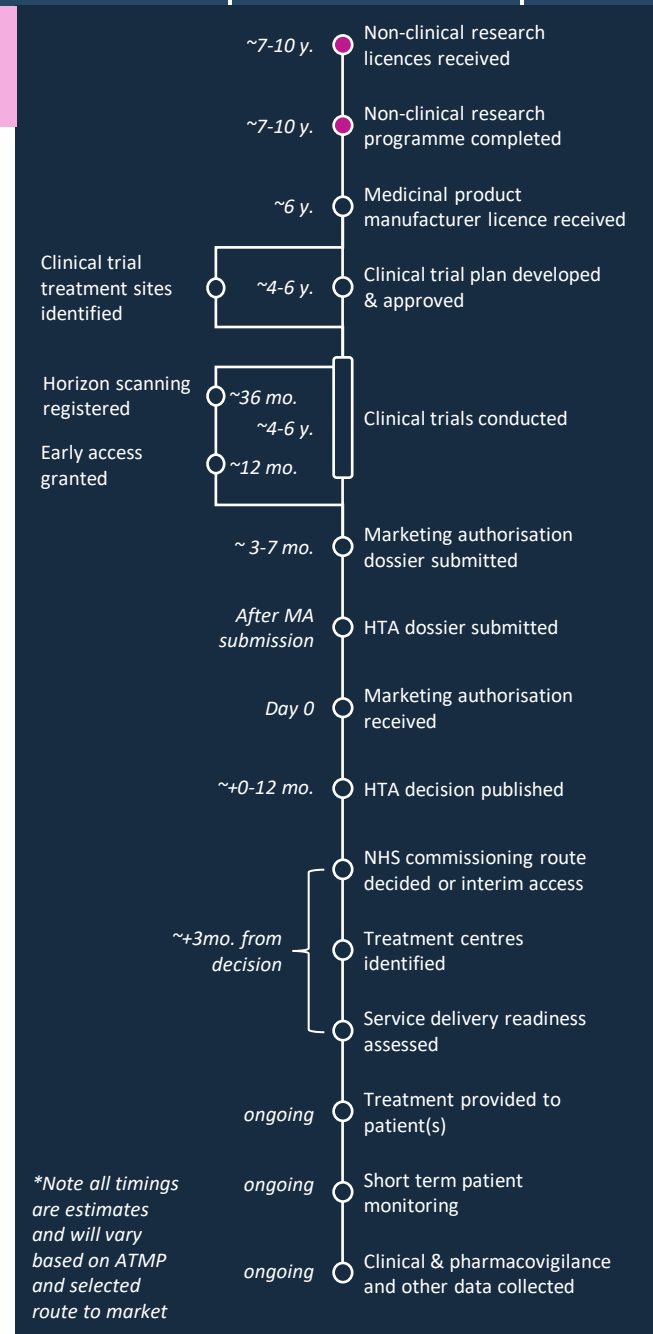
- **GxP compliance & certification**
- Medicinal Product Manufacturer licence(s)
- UKCA marking coordination [if applicable]

Overview | To-do list | **Output**

- Guidance on GMP, GLP, GCP, GPvP and GDP for ATMPs reviewed and assessed
- GLP certification and membership of the UK GLP compliance monitoring programme

Linked steps | Who is involved? | Best practices & tips



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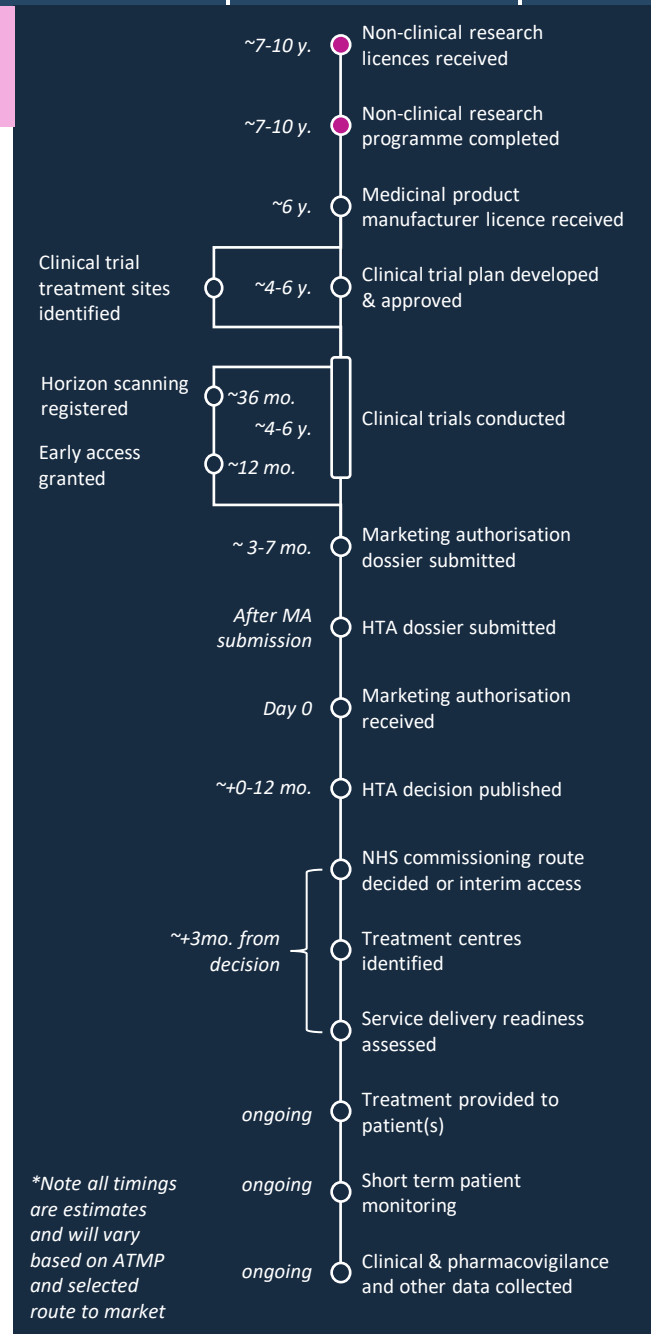
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- UKCA marking coordination [if applicable]

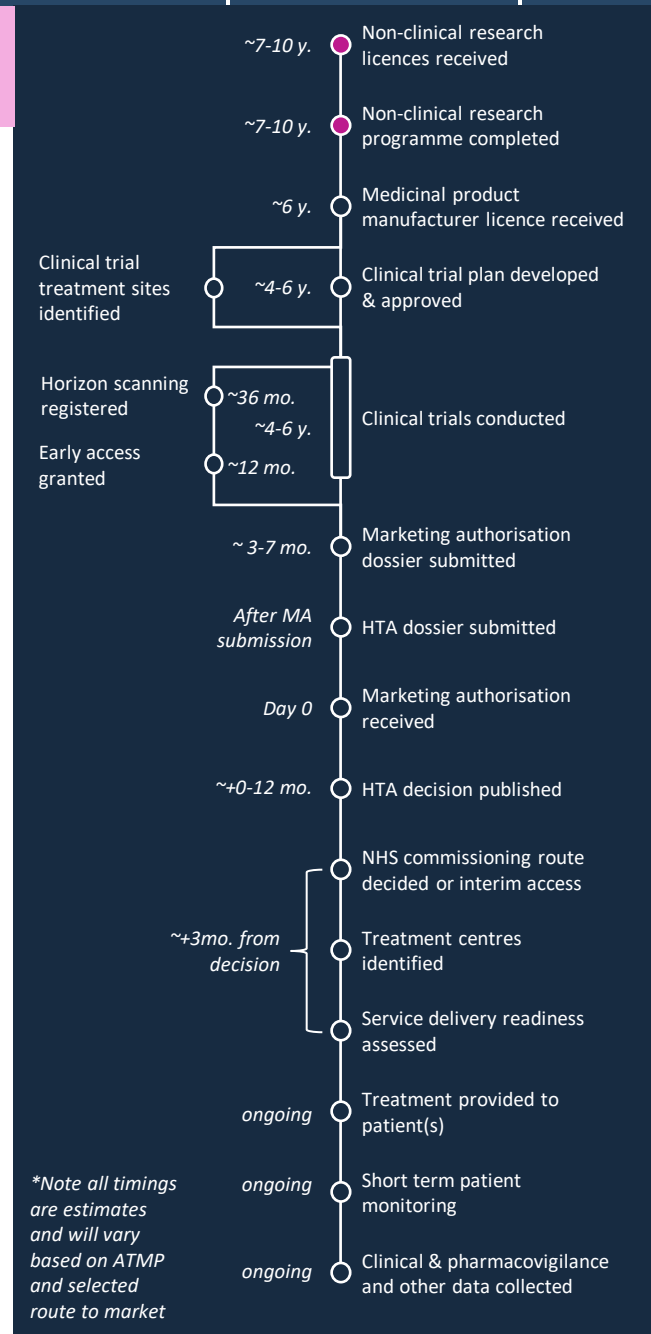
## Overview

## To-do list

## Output

- ATMP developer
- Manufacturing contractor (if applicable)
- Clinical trial sponsor
- MHRA
- UK GLP Monitoring Authority

**Linked steps** **Who is involved?** **Best practices & tips**



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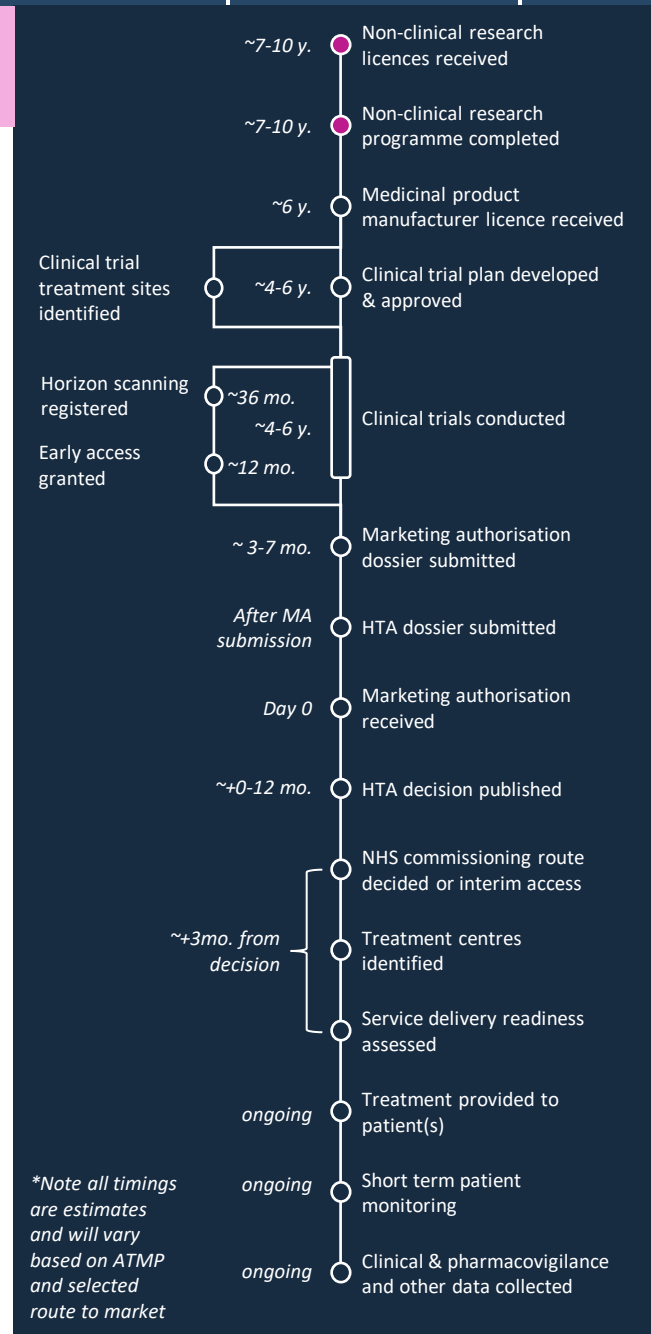
Overview | To-do list | Output

When manufacturing ATMPs for use in humans, key GMP requirements include but are not limited to an ATMP developer's:

- Quality system; premises and equipment; documentation; production and handling of ATMPs; cross contamination; control of starting and raw materials; handling human tissues and cells as starting materials; handling complaint & product recalls; out-of-specification handling; batch release process

Developers can contact the GLPMA at gxplabs@mhra.gov.uk, and contact details for the various MHRA services can be found here

Linked steps | Who is involved? | Best practices & tips



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- **Medicinal Product Manufacturer licence(s)**
- UKCA marking coordination [if applicable]

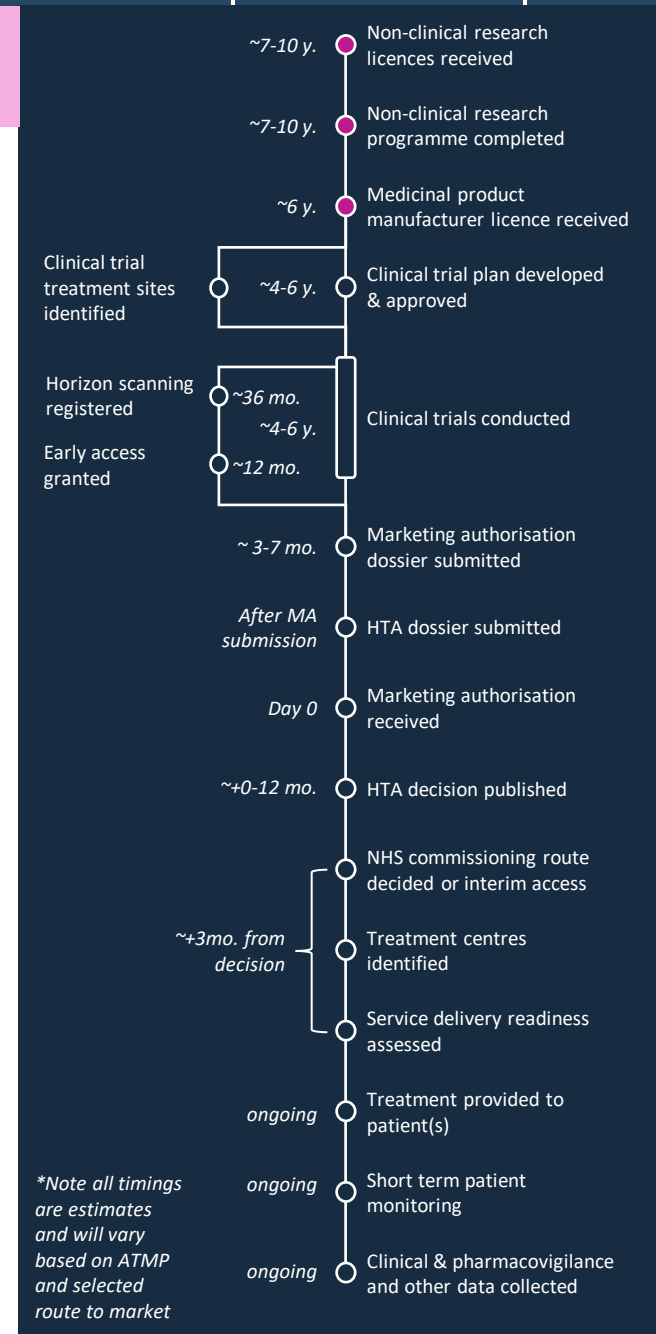
**Overview** | To-do list | Output

ATMP developers must apply to the MHRA for a number of different licences throughout the product journey. A manufacturer licence for for investigational medicinal products (IMP or MIA) must be in place prior to commencement of clinical trials.

Developers must then apply to the MHRA for a licenced product manufacturer/importer licence (also known as Manufacturer Authorisation) prior to Marketing Authorisation submission. Developers should review the Qualified Person (QP) roles and requirements for each licence type.

As part of all licence applications, the MHRA may undertake a site inspection (to confirm compliance with GMP) as part of the licence approval process. There are fees involved for licence applications and inspections.

If outsourcing manufacturing, ensure completion of and supervise/support licensing process by contracted manufacturer.




Linked steps | Who is involved? | Best practices & tips

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- **Medicinal Product Manufacturer licence(s)**
- UKCA marking coordination [if applicable]

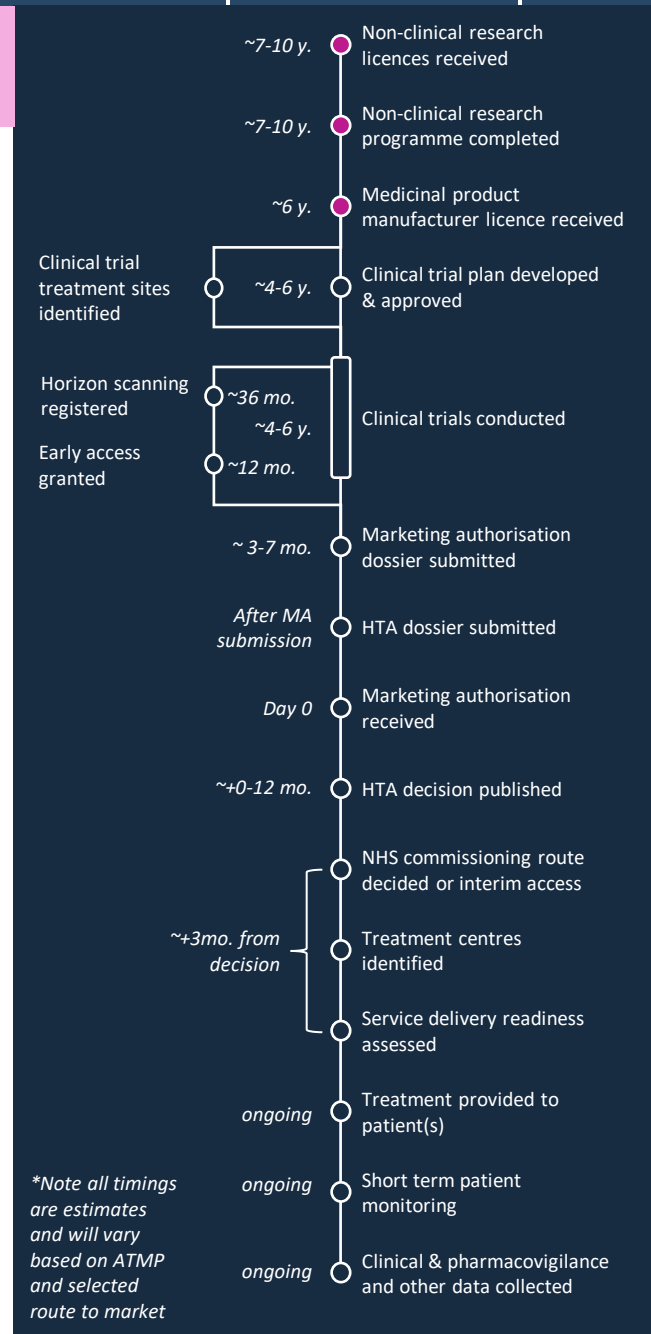
Overview | **To-do list** | Output

- Review MHRA guidance on manufacturer licence applications and determine which licence to apply for here
- Apply for a manufacturer licence for investigational medicinal products (IMP or MIA) to the MHRA here
- Prepare for an MHRA site inspection [if required]
- Apply for a full manufacturer/importer licence here
- Further guidance from the MHRA on QP, QC and other requirements for a manufacturer/importer licence holder can be found here
- Review ATTC guidance on the role of the QP with ATMPs here

**When**

Manufacturer licence for investigational medicinal products must be granted prior to commencement of clinical trials. Licence applications to the MHRA typically take 90 days. Full manufacturer/importer licence application must be submitted prior to MA submission

**Linked steps** | **Who is involved?** | **Best practices & tips**



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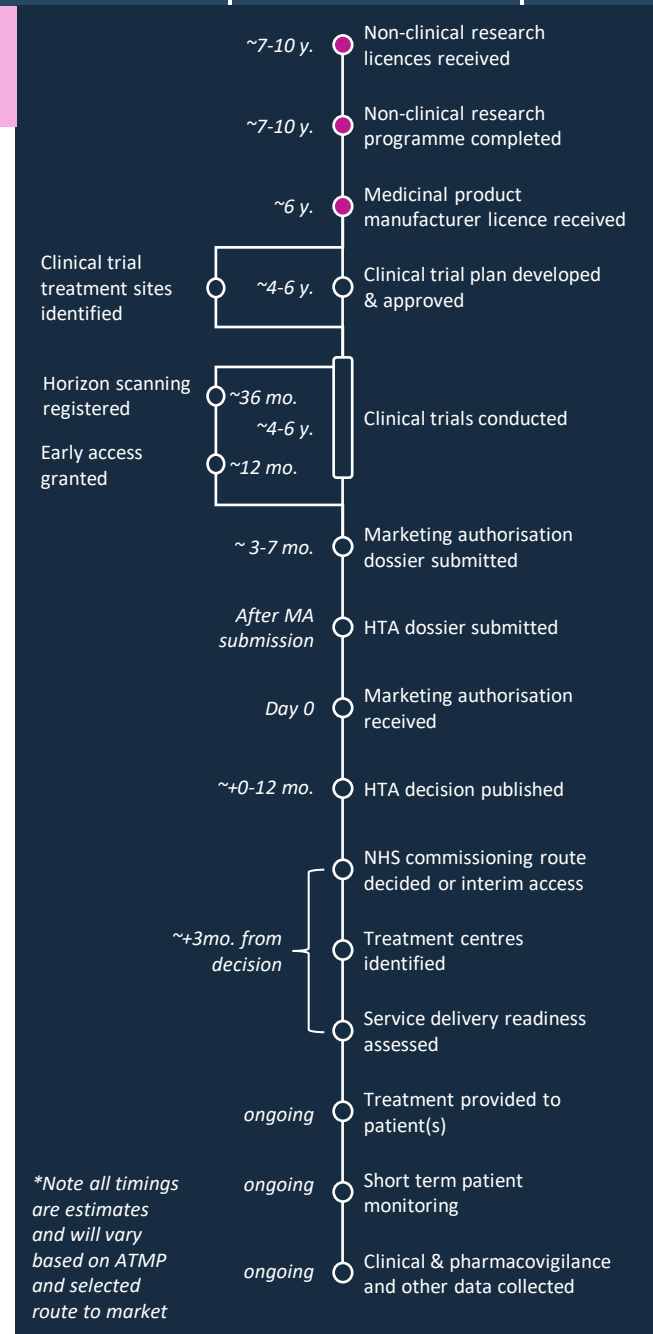
- **Medicinal Product Manufacturer licence(s)**
- UKCA marking coordination [if applicable]

Overview | To-do list | **Output**

- Manufacturer licence for investigational medicinal products from the MHRA
- Medicinal product manufacturer/importer licence from the MHRA

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- UKCA marking coordination [if applicable]

## Overview

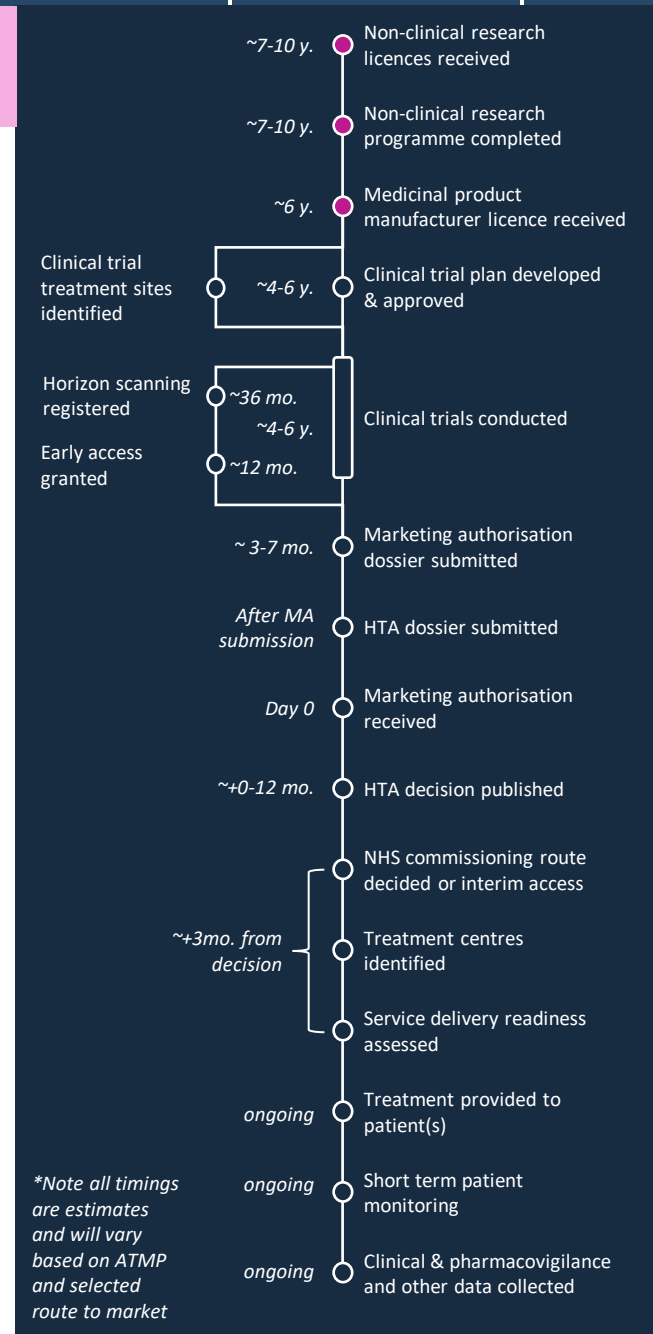
## To-do list

## Output

GxP compliance & certification

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- **Medicinal Product Manufacturer licence(s)**
- UKCA marking coordination [if applicable]

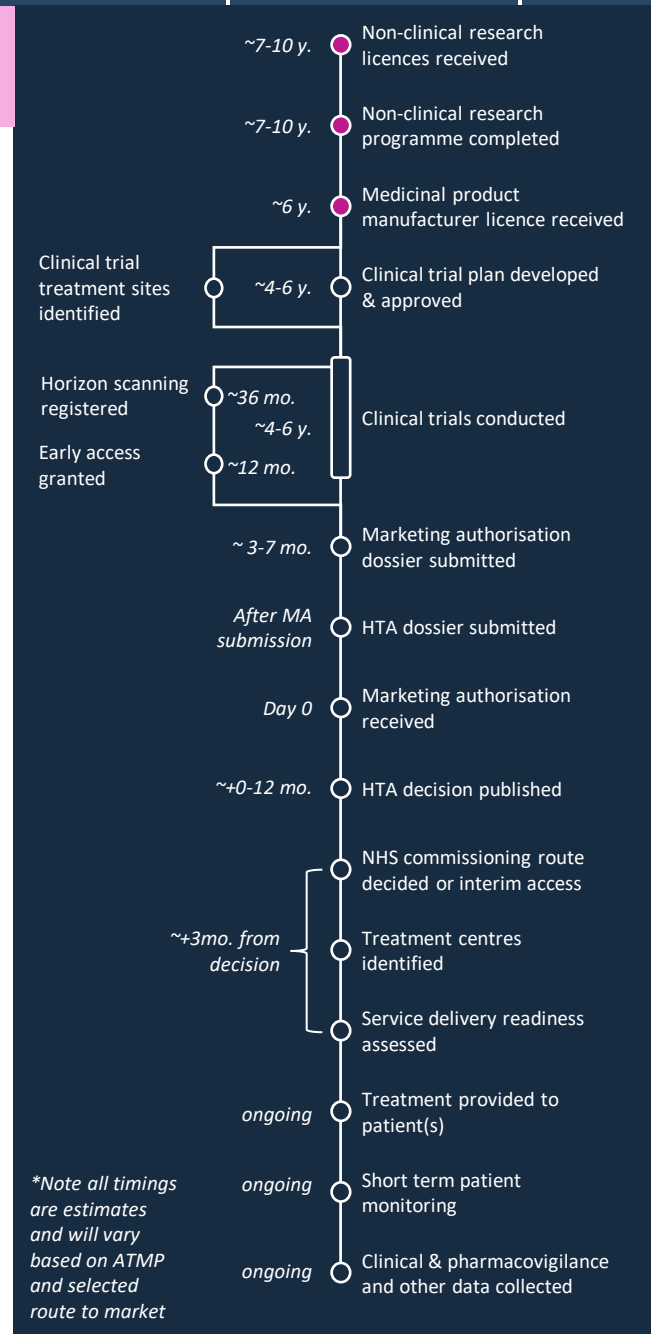
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- Manufacturing contractor (if applicable)

**Linked steps** **Who is involved?** **Best practices & tips**



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- UKCA marking coordination [if applicable]

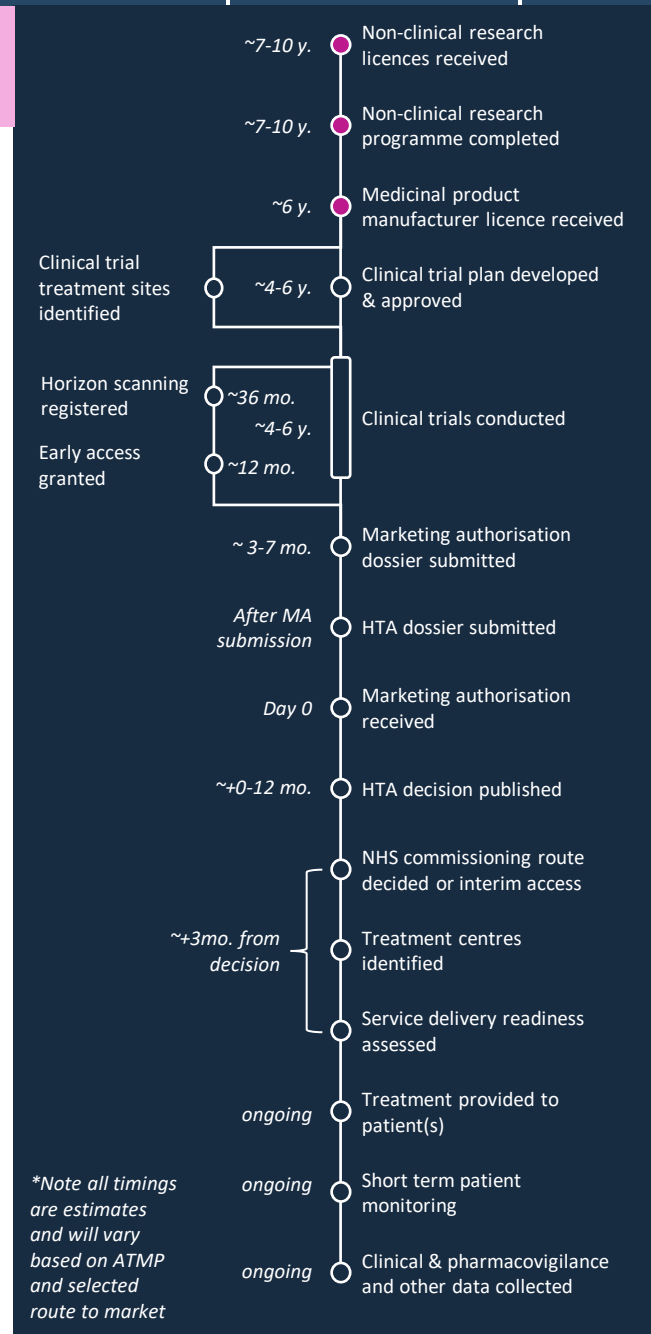
## Overview

## To-do list

## Output

- For queries relating to licensing, contact the MHRA at pcl@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



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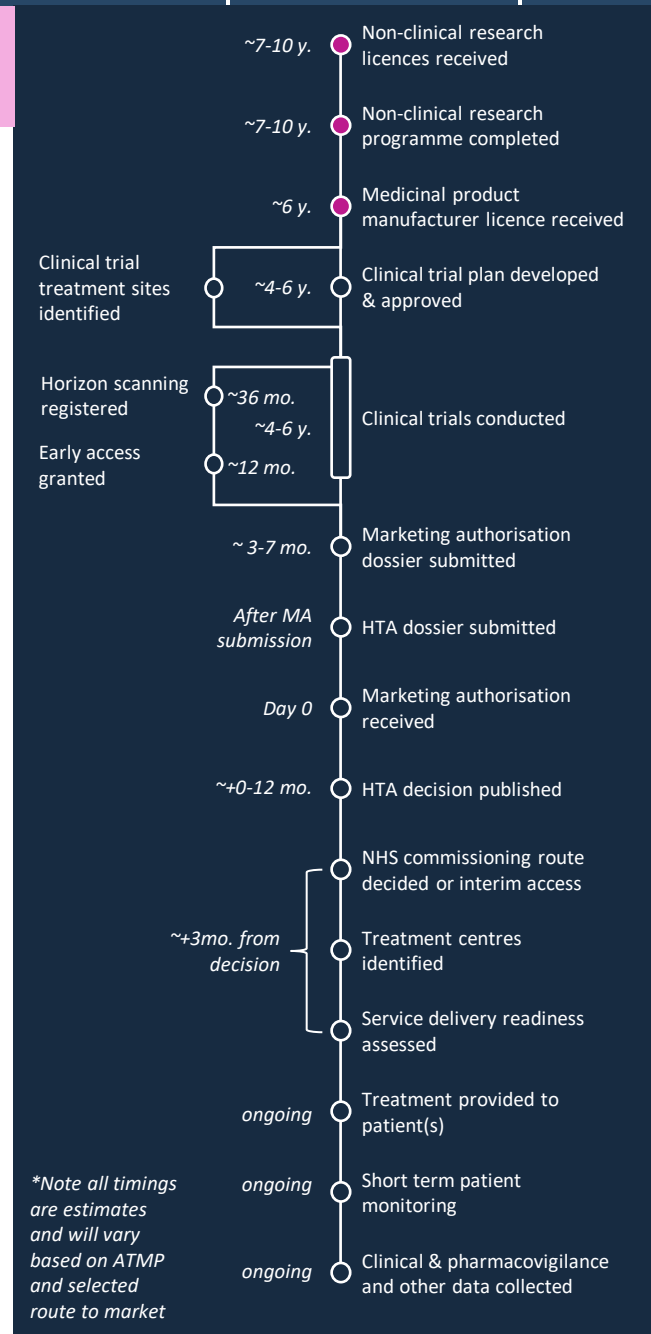
- **UKCA marking coordination [if applicable]**

**Overview** | To-do list | Output

For combination ATMPs which include a medical device component, developers will need to coordinate UKCA marking (and/or CE marking if in Northern Ireland or for use of the product in the EU) in order to use their device component. There may be fees involved for these services.

Developers can also request regulatory advice from the MHRA regarding medical device requirements if required.

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- **UKCA marking coordination [if applicable]**

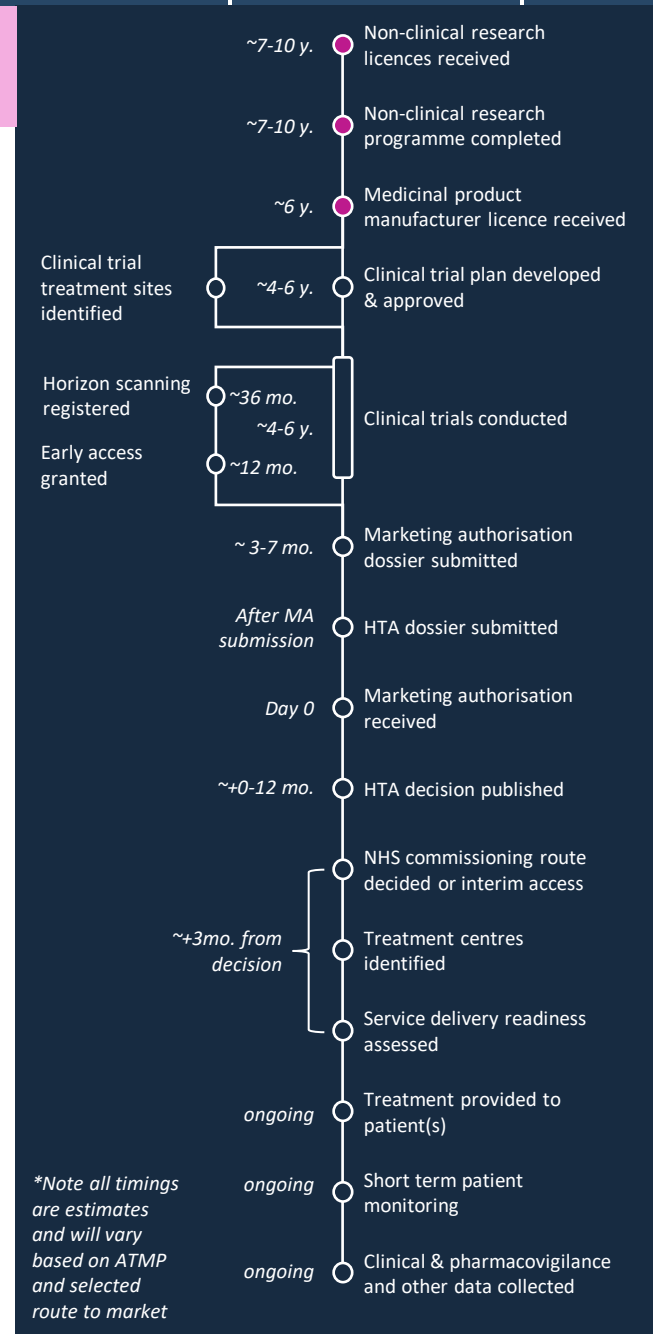
Overview | **To-do list** | Output

- Review medical device regulatory requirements here
- EMA guidance on performing a conformity assessment for CE marking can be found here
- Request regulatory advice from the MHRA here (if required), the MHRA may recommend a UK Approved Body for use in conformity assessment
- For novel medical devices, a clinical investigation for a medical device may be required, see guidance here
- Class I devices and general IVD manufacturers can self-certify against the UKCA mark
- [If applicable] Identify UK Approved Body to request conformity assessment
- Full list of UK Market Conformity Assessment Bodies can be found here

**When**

During R&D phase and prior to commencing clinical trials

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What licences and/or approvals are required to conduct research?**

2 What key regulatory steps are required to receive marketing authorisation?

3 What programmes are available to accelerate time to market?

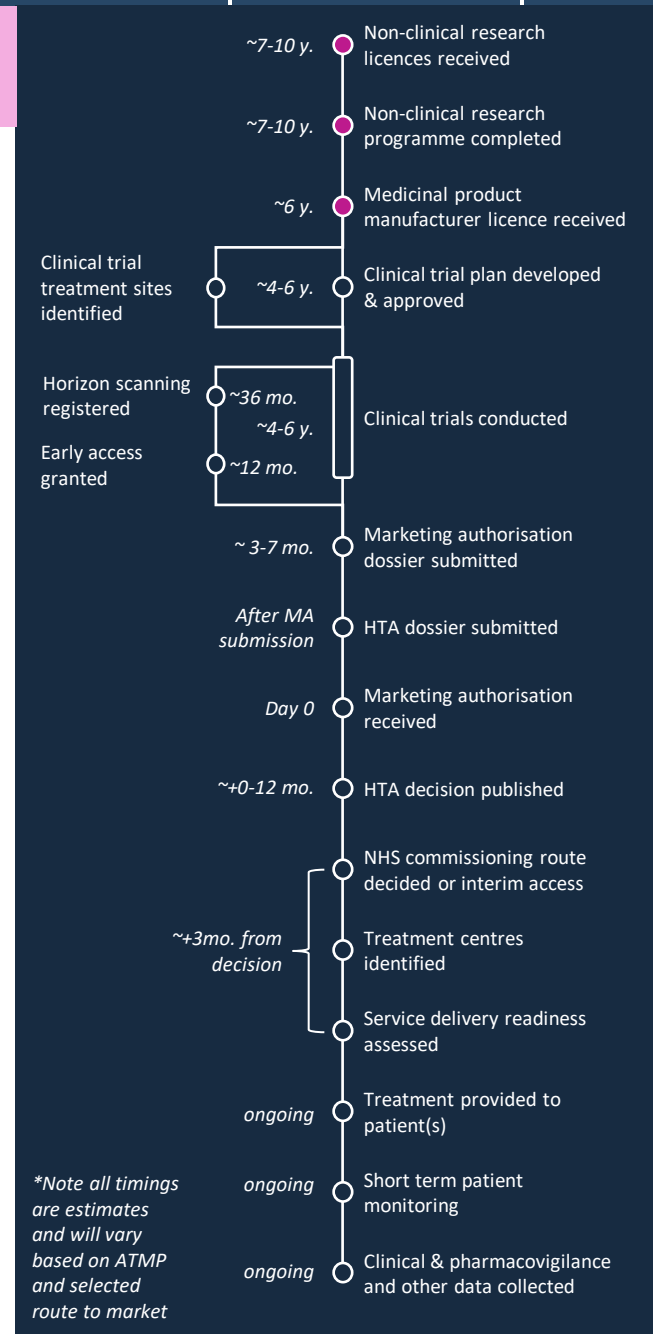
## KEY TOPICS

- Genetically Modified Organisms notification [if applicable]
- Human Tissue Authority licence
- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- **UKCA marking coordination [if applicable]**

Overview | To-do list | **Output**

- UKCA and/or CE marking for medical device component

**Linked steps** | **Who is involved?** | **Best practices & tips**



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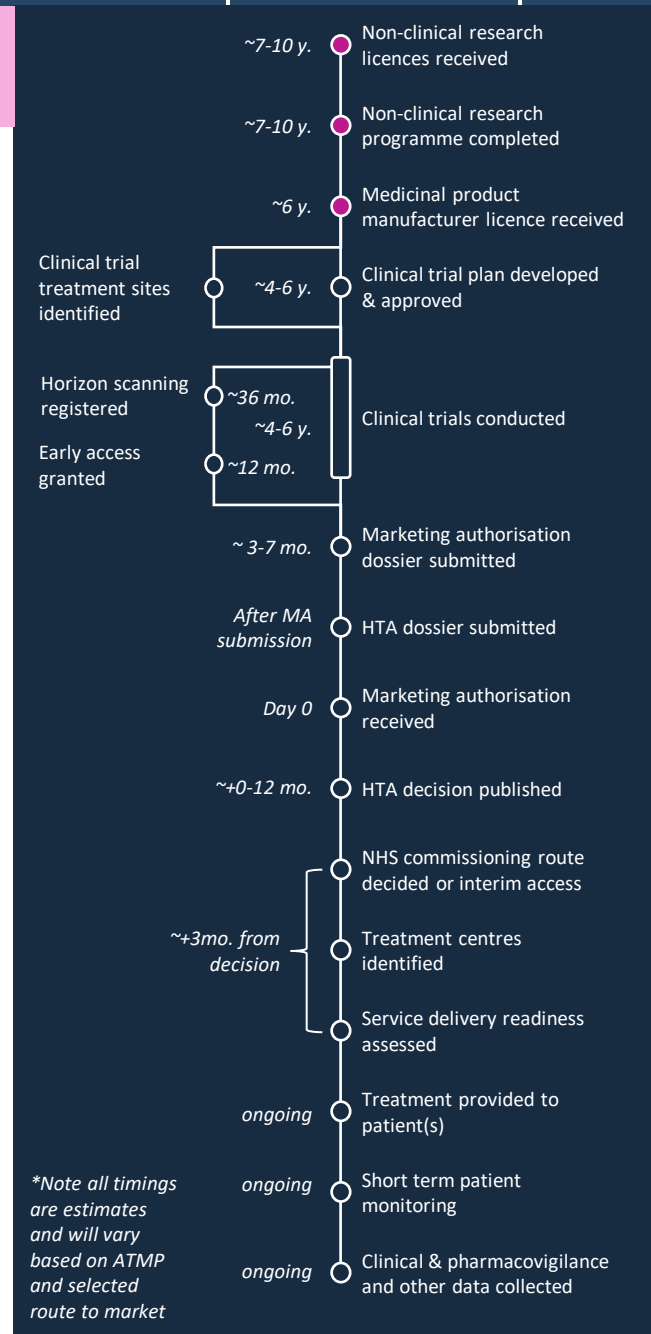
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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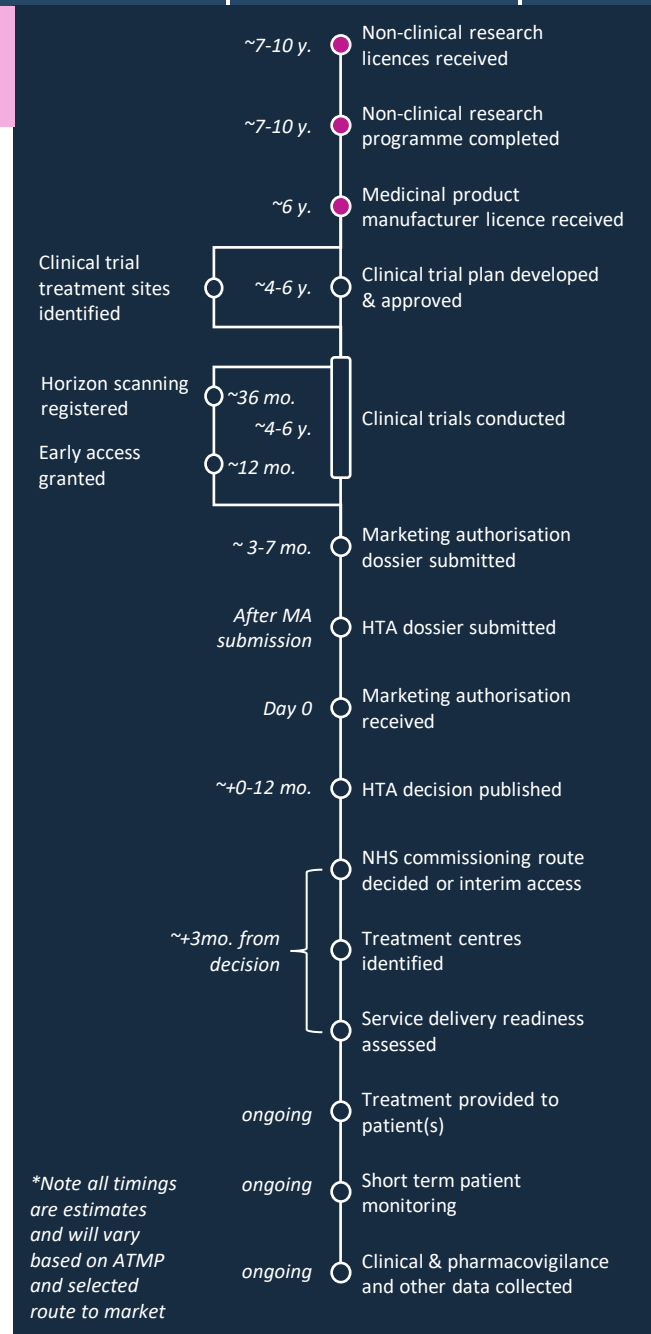
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- EMA

**Linked steps** **Who is involved?** **Best practices & tips**



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- GxP compliance & certification
- Medicinal Product Manufacturer licence(s)
- **UKCA marking coordination [if applicable]**

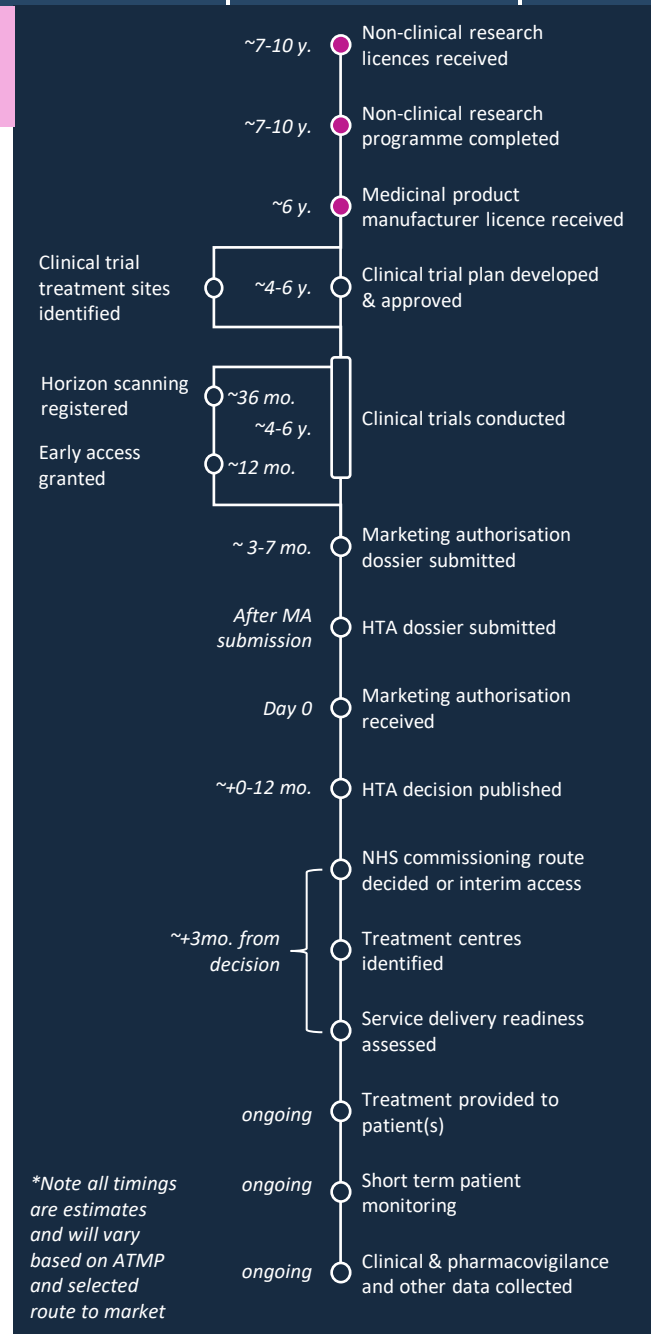
## Overview

## To-do list

## Output

- For queries relating to medical devices, contact the MHRA at devices.regulatory@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS



**Overview** | To-do list | Output

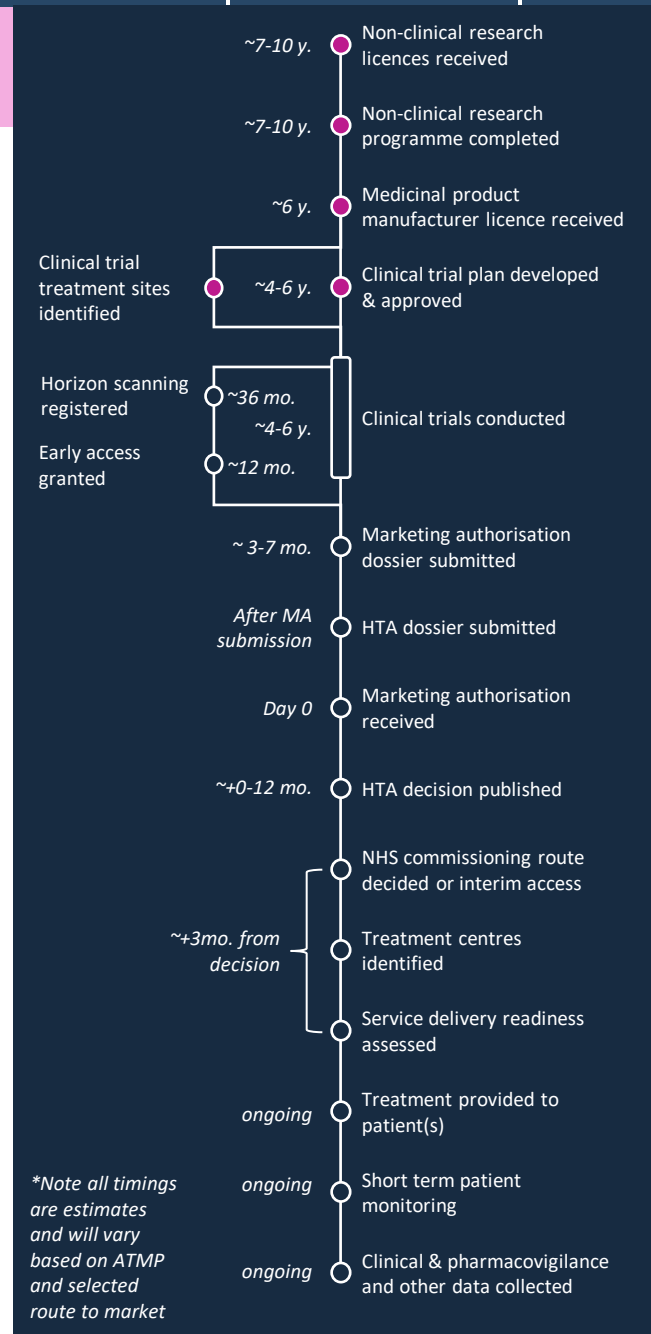
Paediatric Investigational Plans (PIP) [or submission of a waiver for non-paediatric products] are required to be submitted to the MHRA for all products and are required at the point of first-in-human (FIH) trial and no later than before commencement of confirmatory trials. Completion of a PIP or waiver is a condition for receiving Marketing Authorisation.

Prior to submission of Marketing Authorisation, developers are required to complete a PIP compliance check to verify completion and submission of their PIP.

EU-PIPs, modifications and full product specific waivers with an EMA decision agreed before 1 January 2021, will be adopted as UK-PIPs on or after that date

Note: for developers based in Northern Ireland, PIPs must be submitted to both the EMA and MHRA.

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

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3 What programmes are available to accelerate time to market?

## KEY TOPICS

- **Paediatric Investigational Plans approval**
- Regulatory approval route selection
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]
- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

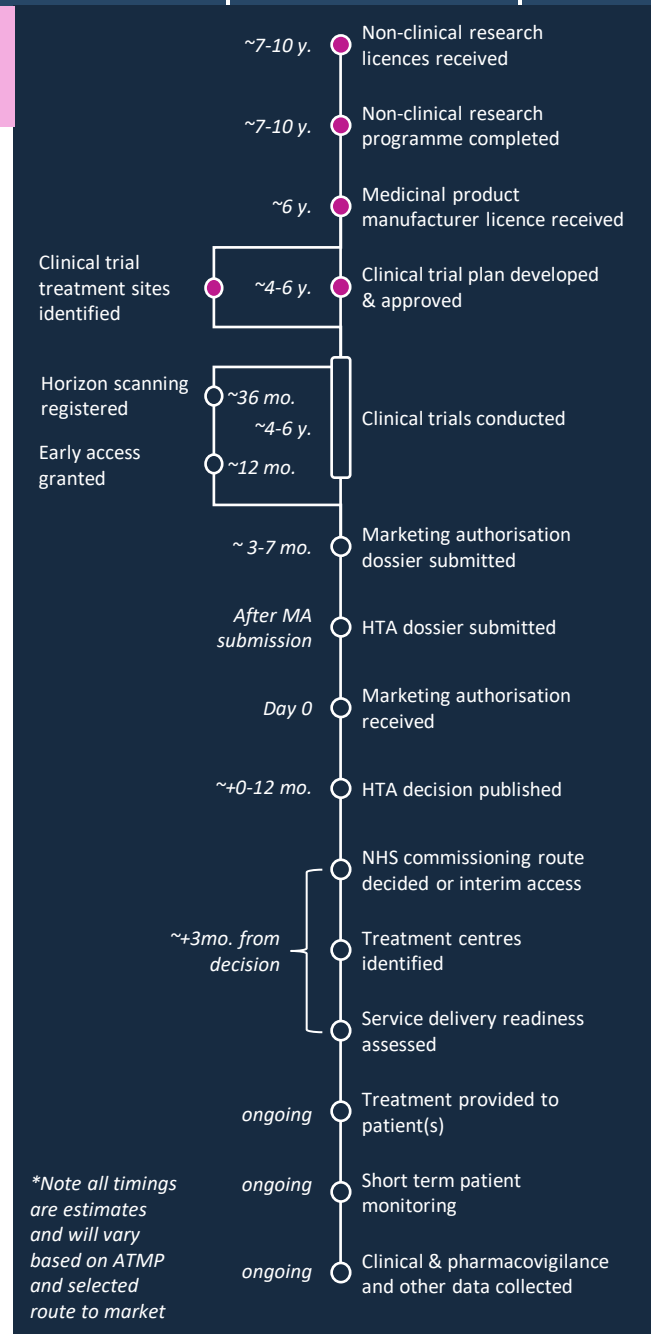
Overview | **To-do list** | Output

- Review guidance on procedures for UK Paediatric Investigation Plans here
- Submit PIP to the MHRA via the submissions portal
  - Review process and register for access to the MHRA submissions portal here
- For Northern Ireland, submit the PIP to the MHRA (via submissions portal) and the EMA (via EMA eSubmission gateway)
  - EMA guidance on PIPs can be found here
  - Further guidance and templates to submit via the EMA eSubmission gateway here
- Complete a UK PIP compliance check prior to Marketing Authorisation submission, guidance from MHRA here

**When**

- Initial PIP submission should be completed at Phase I trials
- PIP compliance check must be completed after the last study listed in the PIP completed at least 60 days prior to the intended Marketing Authorisation submission

**Linked steps** | **Who is involved?** | **Best practices & tips**



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## KEY TOPICS

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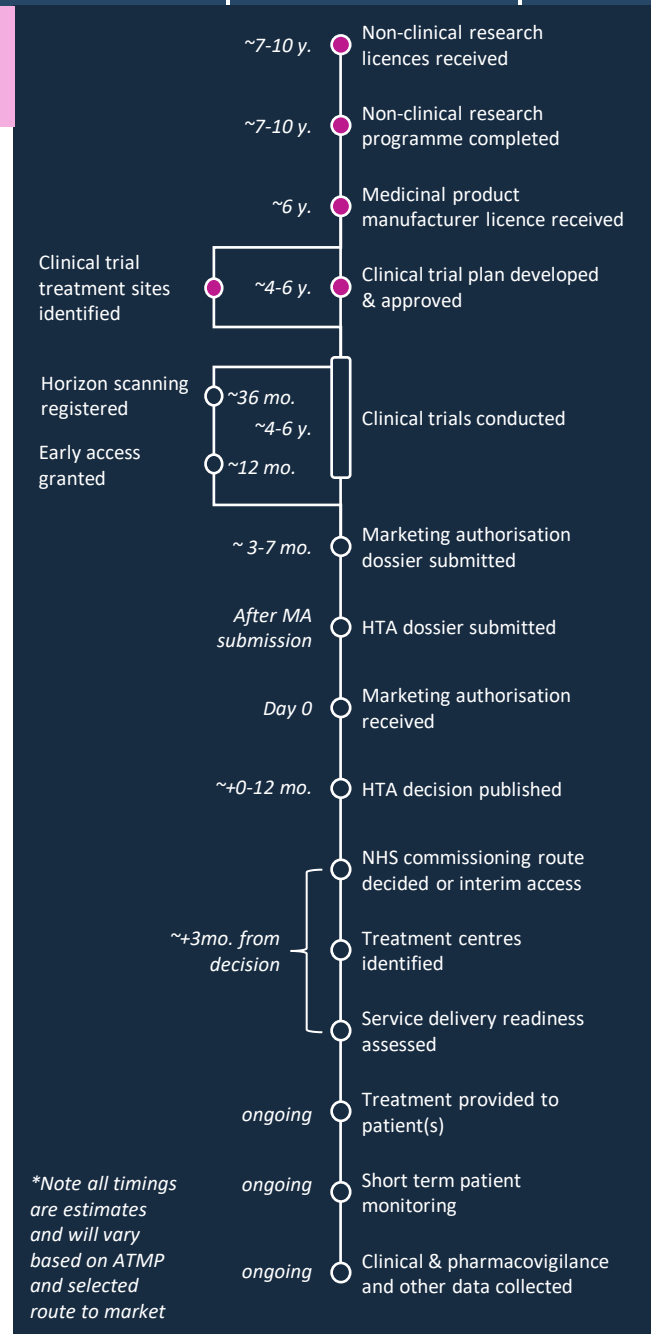
- Marketing Authorisation submission
- Post-authorisation compliance

Overview | To-do list | **Output**

- Paediatric Investigation Plan (PIP) [or waiver] submitted
- UK PIP compliance check complete




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

1 What licences and/or approvals are required to conduct research?

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- Marketing Authorisation submission
- Post-authorisation compliance

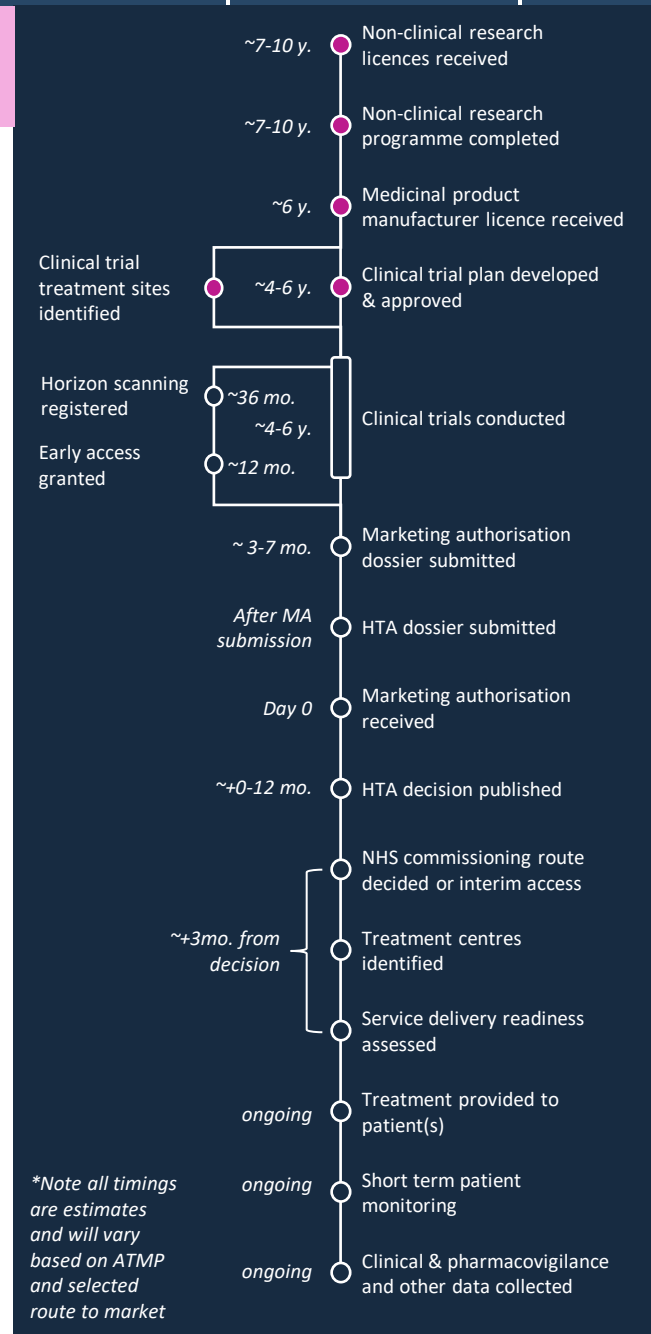
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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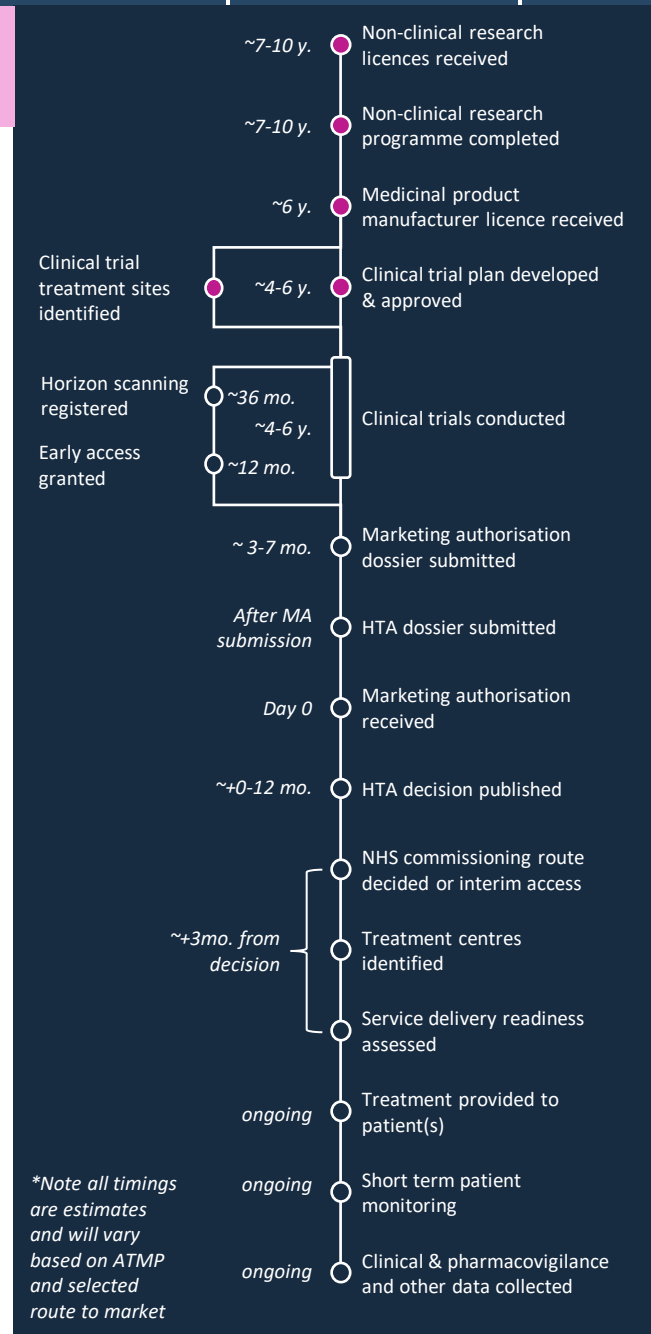
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- EMA

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

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- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

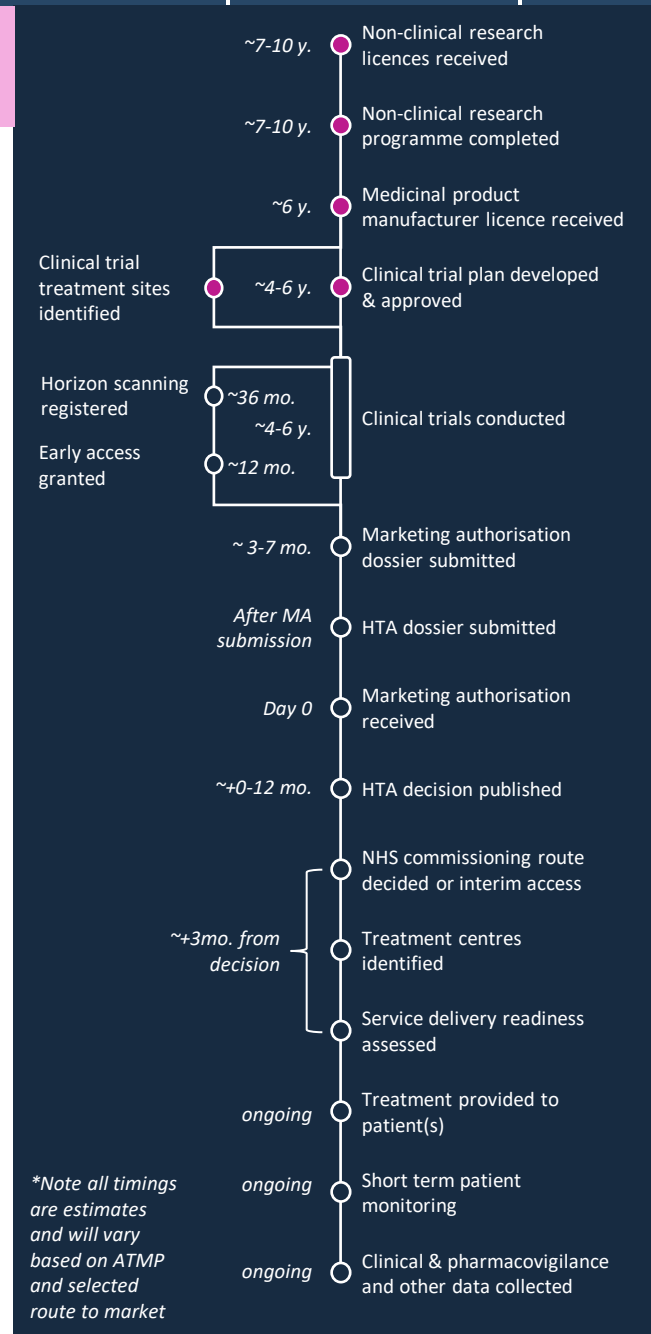
## Overview

## To-do list

## Output

- It is essential that developers ensure that their PIP and their compliance check have been completed in advance of Marketing Authorisation submission, as absence of a PIP can cause delays to Marketing Authorisation.
- For enquiries about paediatric submissions, contact the MHRA Paediatric Unit at ukpip@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



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- Marketing Authorisation submission planning
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- Post-authorisation compliance

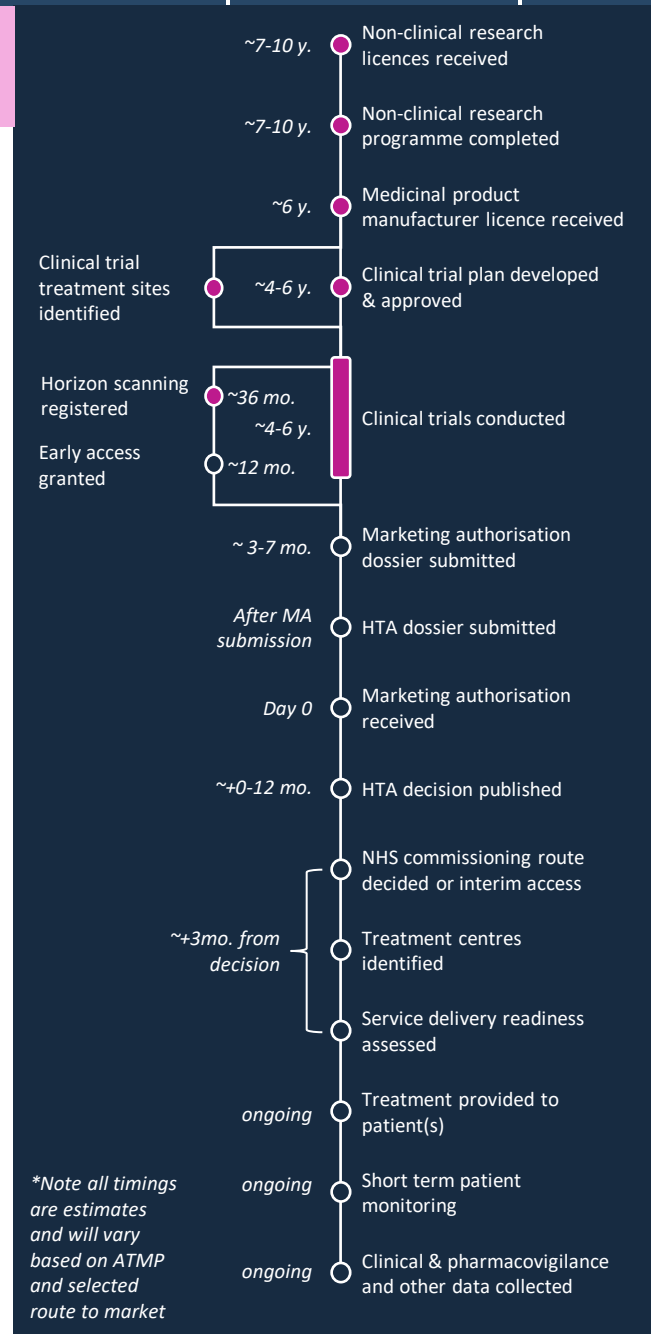
**Overview** | To-do list | Output

Developers should review the various routes for Marketing Authorisation applications available to them to understand the process involved and determine which route is most applicable.

These routes include but may not be limited to; 150 day assessment, Rolling Review, EC decision reliance, Project Orbis and Access Consortium.
There are also some flexibilities to the Marketing Authorisation routes, such as the Conditional MA and MA under exceptional circumstances.

In exceptional circumstances, developers may choose to provide their product without a Marketing Authorisation through the unlicenced route. They should review the MHRA guidance on providing unlicenced products and consider if a "specials" or "hospital exemption" licence is most applicable and make the relevant application. There are fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- Paediatric Investigational Plans approval
- **Regulatory approval route selection**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]
- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

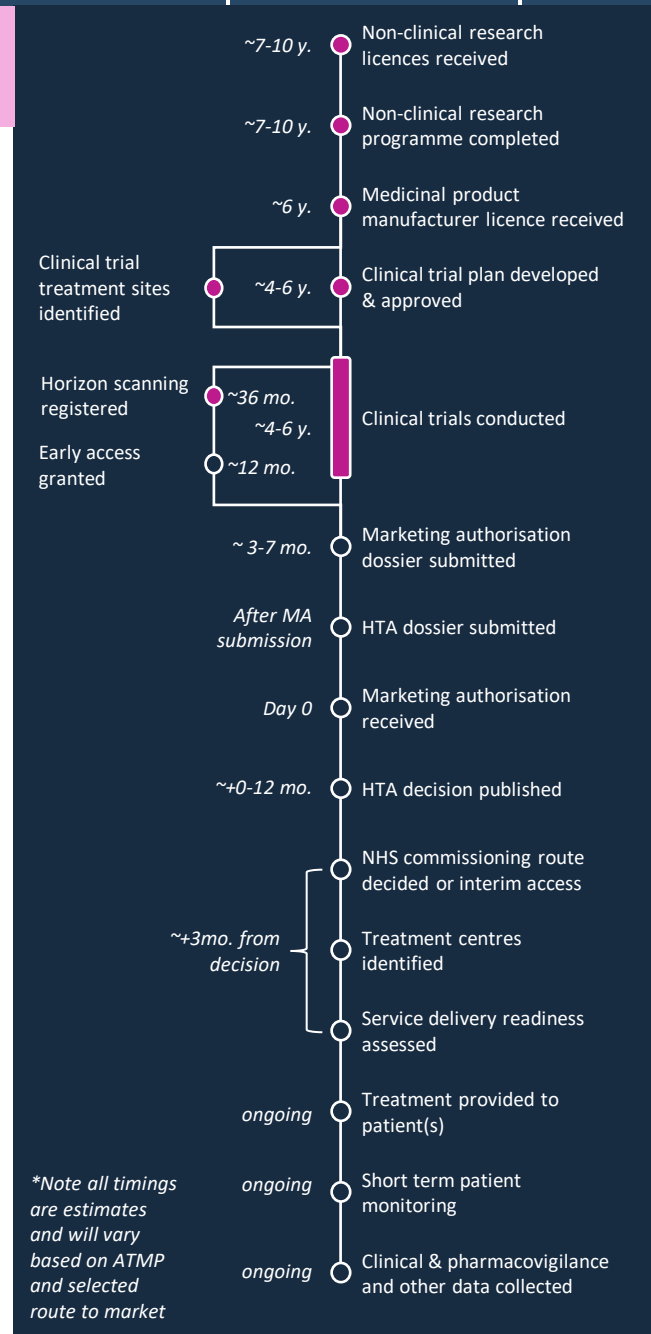
Overview | **To-do list** | Output

- Review the various different Marketing Authorisation routes and guidelines for unlicenced products and select which route to follow
- Marketing Authorisation routes:
  - See 150 day assessment guidance here
  - See rolling review guidance here
  - See EC decision reliance guidance here
  - See Project Orbis guidance here
  - See Access Consortium guidance here
- See Conditional marketing authorisation and exceptional circumstances guidance here
- [If applicable] Review the MHRA guidance on providing unlicenced products here and consider if "specials" or "hospital exemption" is most applicable
  - See specials guidance here
  - Review Specials ATMP flowchart here
  - See hospital exemption guidance here
- [If applicable] Apply to the MHRA for the relevant licence type here

**When**

Prior to Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips



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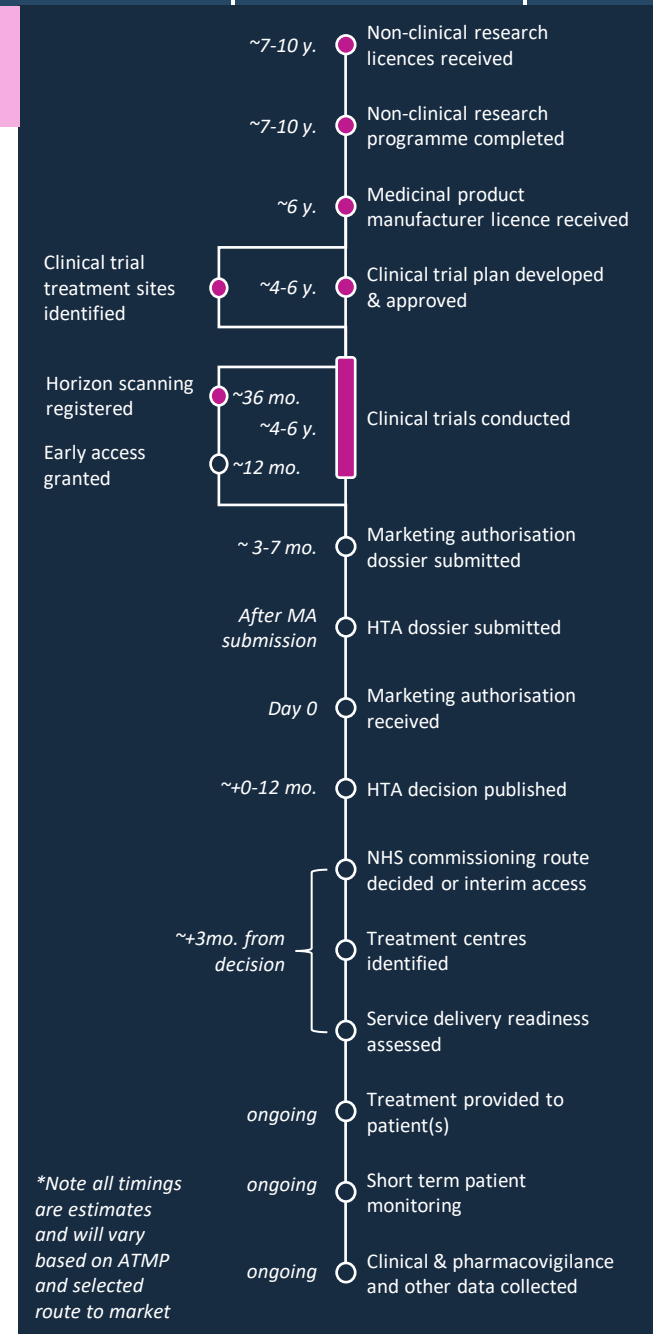
- Post-authorisation compliance

Overview | To-do list | **Output**

- Decision on planned route for regulatory approval




Linked steps | Who is involved? | Best practices & tips

1 What licences and/or approvals are required to conduct research?

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## KEY TOPICS

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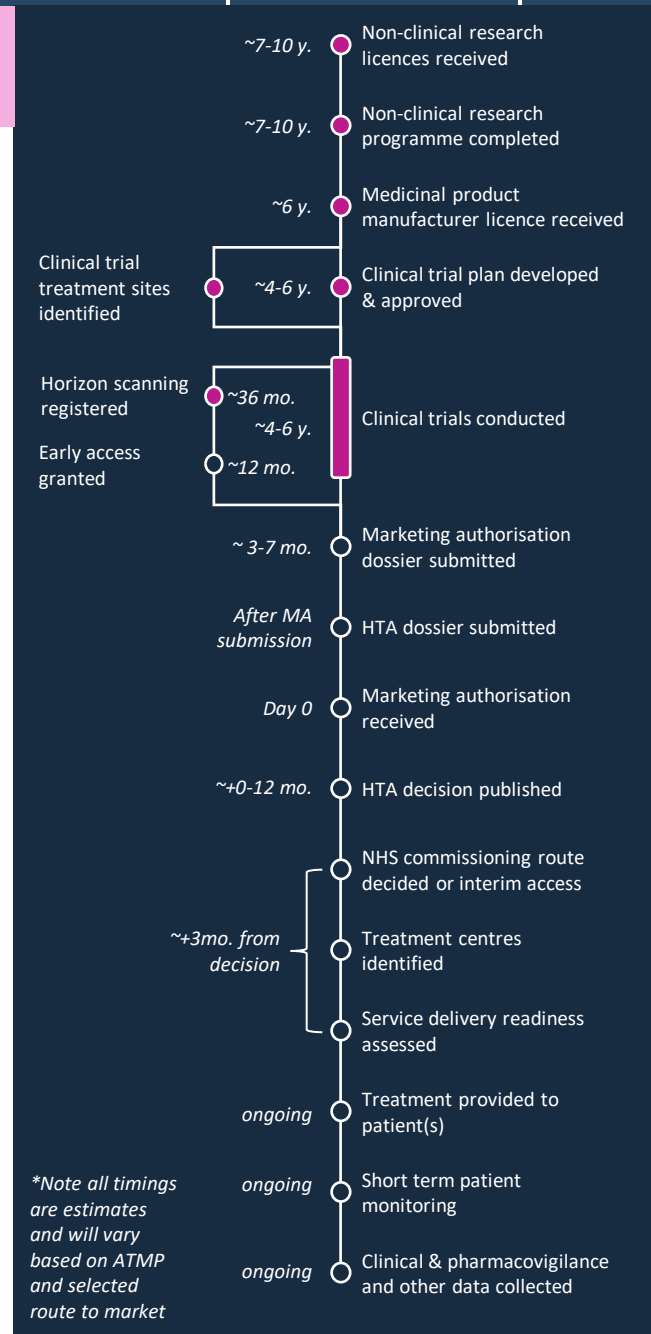
## Overview

## To-do list

## Output

- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Regulatory and/or scientific advice

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- Post-authorisation compliance

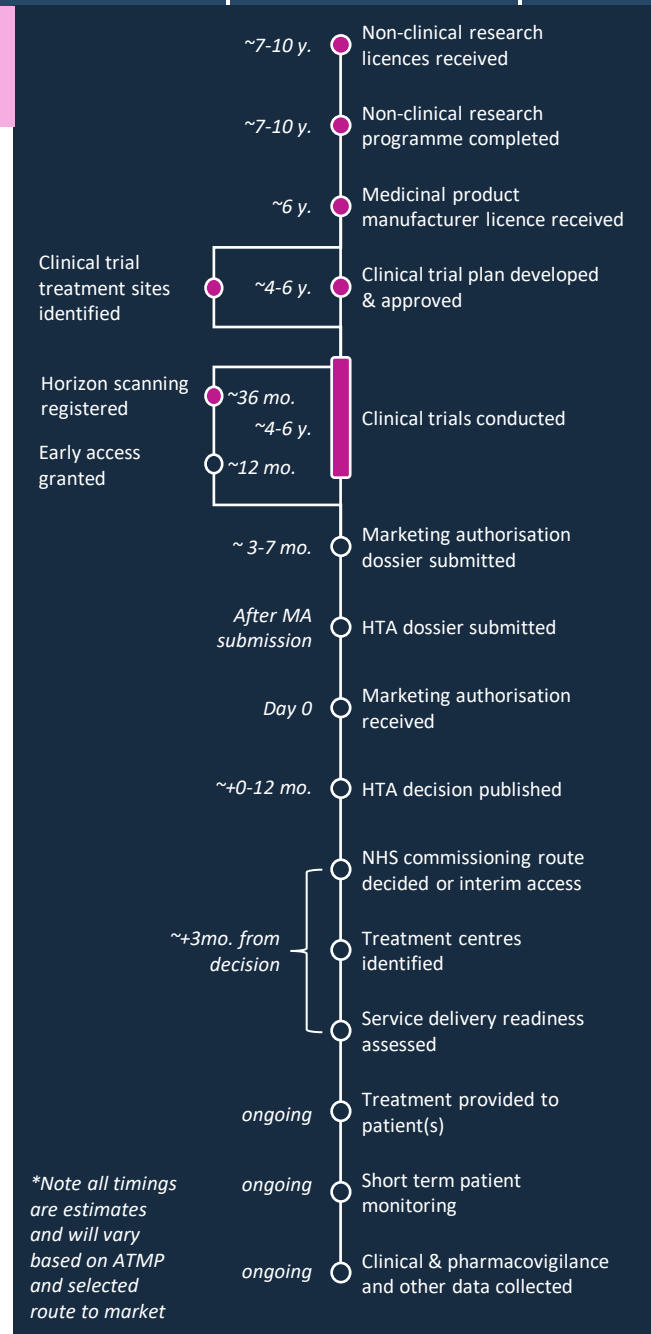
## Overview

## To-do list

## Output

- ATMP developer
- MHRA

**Linked steps** **Who is involved?** **Best practices & tips**



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- Marketing Authorisation submission planning
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- Post-authorisation compliance

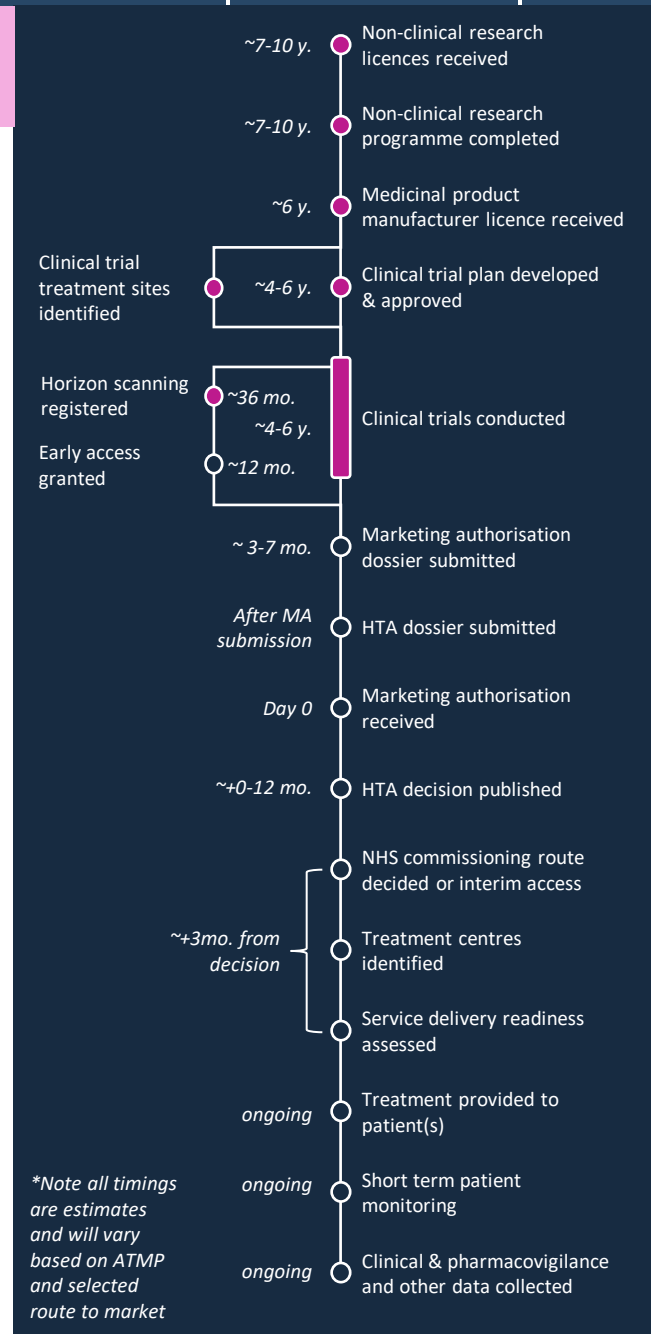
## Overview

## To-do list

## Output

- Engage with MHRA to discuss options early and inform them of intended route (once confirmed), contact details for the MHRA can be found here
- Developers should consider their marketing strategy early and reflect ambitions (and timelines) for the product in chosen route to market

**Linked steps** **Who is involved?** **Best practices & tips**



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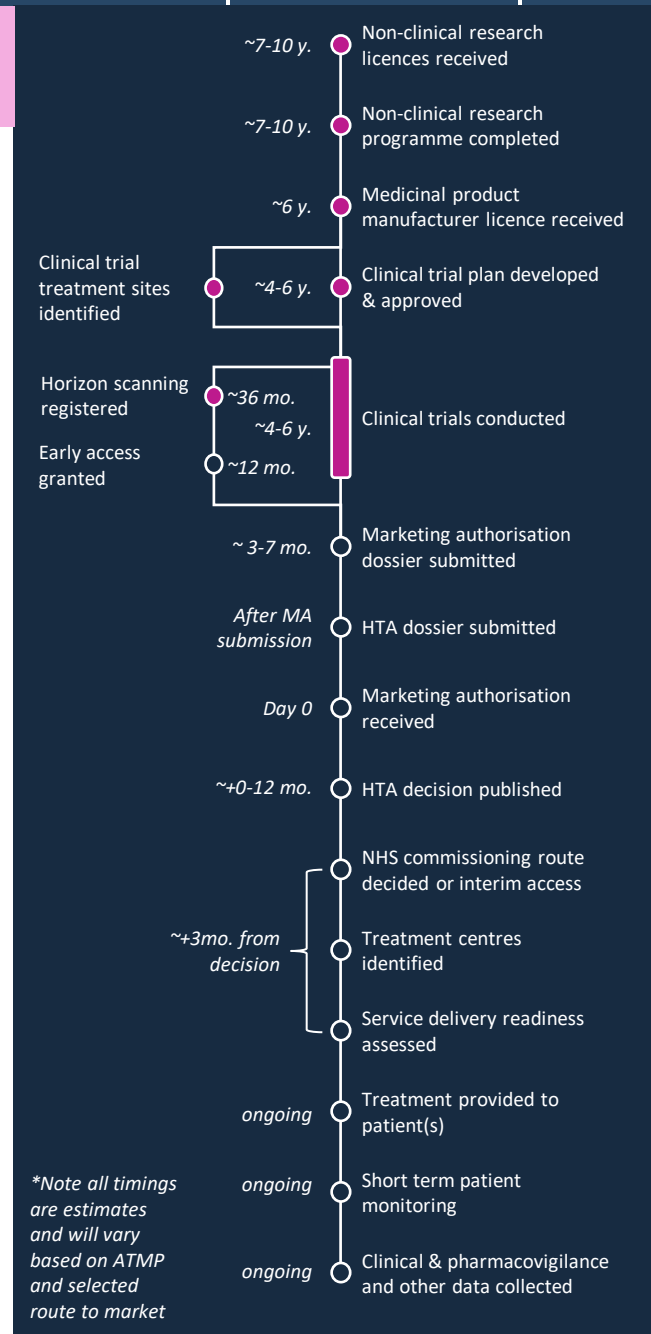
- International marketing authorisation coordination via Access Consortium [optional]
- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

**Overview** | To-do list | Output

Developers of oncology products may submit a request to the MHRA to recommend their product for Project Orbis. Co-ordinated by the FDA, Project Orbis provides a route for concurrent review of marketing authorisation applications for promising cancer medicines from participating countries.

Applicants for Project Orbis are required to have an innovation passport designation, and will still be required to submit their full Marketing Authorisation to the MHRA using their existing process. There are fees involved for these services.




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

## KEY TOPICS



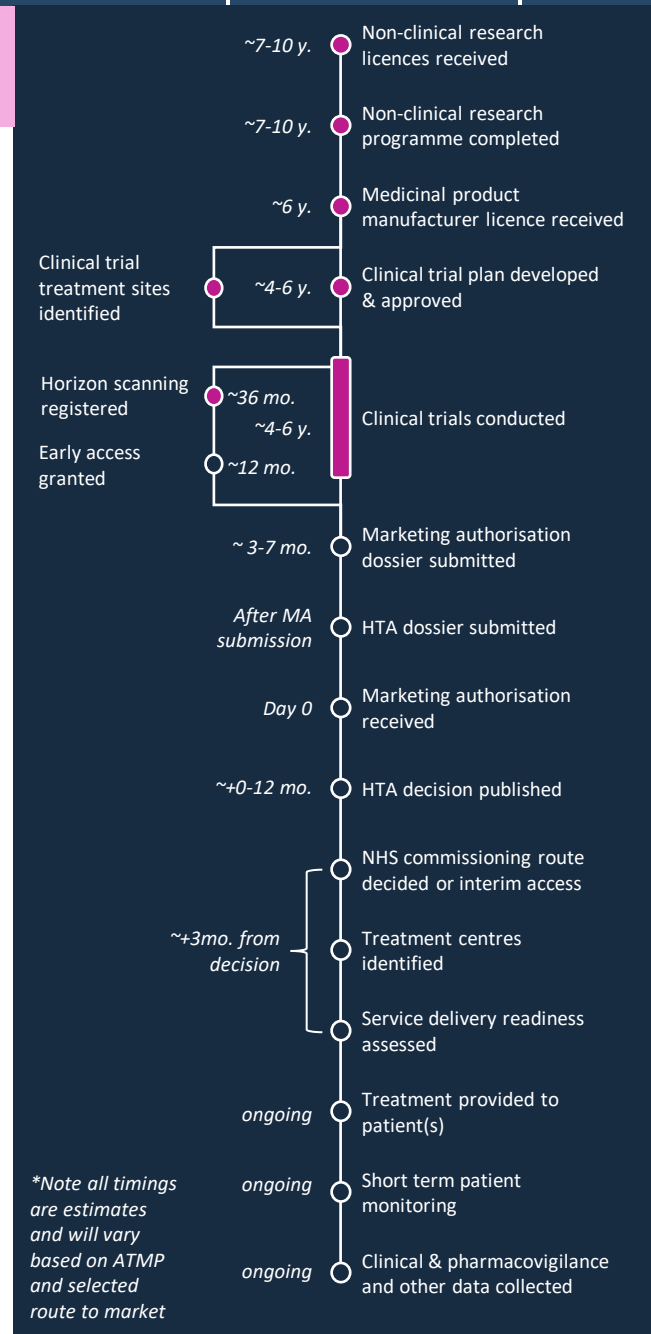
Overview | **To-do list** | Output

- Review Project Orbis guidance here and determine which submission type to use
- If not already completed, submit application through ILAP for Innovation Passport designation here
- Submit request (including a summary of the product and details of eligibility criteria) to the MHRA for them to recommend inclusion in Project Orbis to the FDA via Orbis-MHRA@mhra.gov.uk
- Submit meeting request to MHRA regarding Project Orbis submission via Orbis-MHRA@mhra.gov.uk
- Continue UK submission process along with concurrent submissions with participating countries
- Receive outcome decision from the FDA

**When**

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

**Linked steps** | **Who is involved?** | **Best practices & tips**



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## KEY TOPICS

- Paediatric Investigational Plans approval
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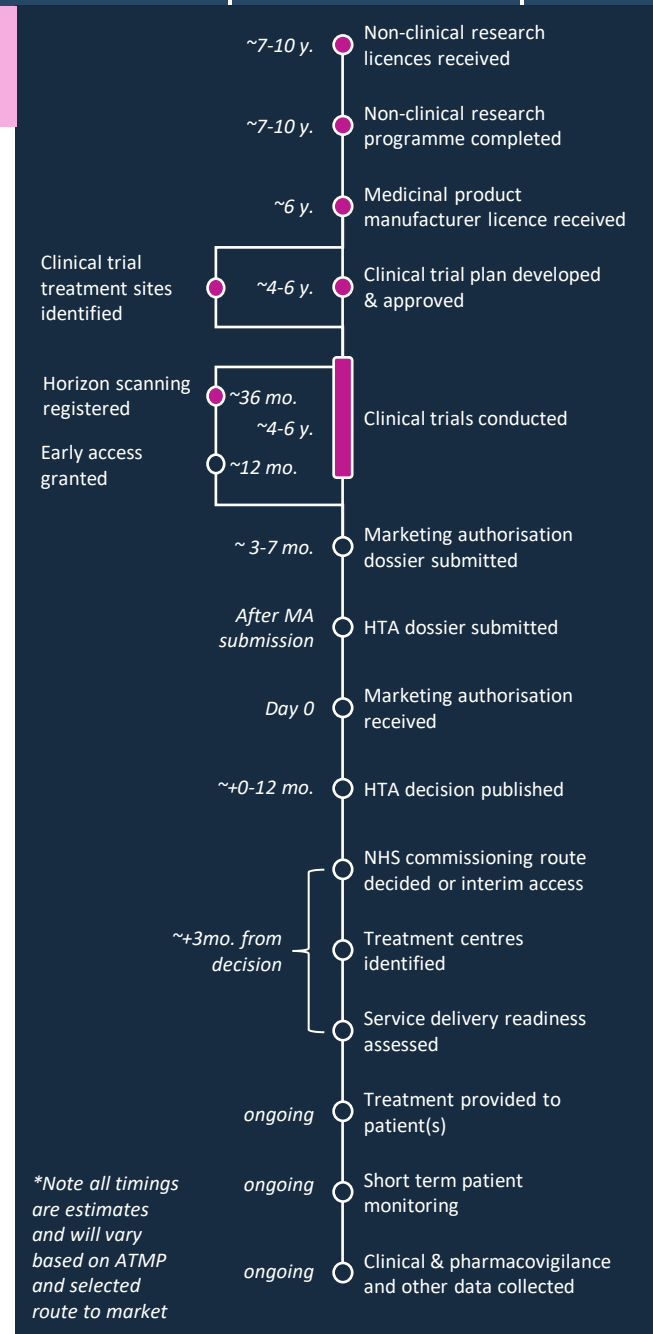
- International marketing authorisation coordination via Access Consortium [optional]
- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

Overview | To-do list | **Output**

- Inclusion or exclusion decision from FDA
- Marketing Authorisation decision from all participating Project Orbis countries

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

Marketing Authorisation submission

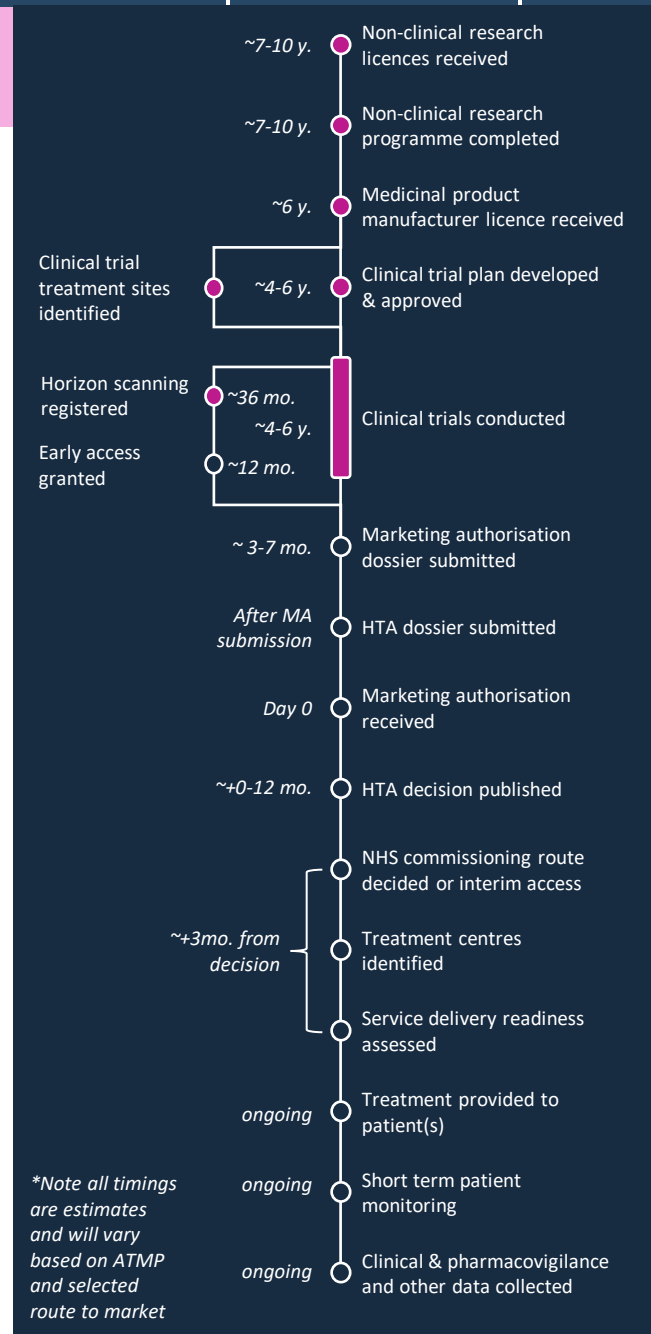
Innovative Licensing and Access Pathway (ILAP) [optional]

Regulatory and/or scientific advice

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

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- International marketing authorisation coordination via Access Consortium [optional]
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- Post-authorisation compliance

## Overview

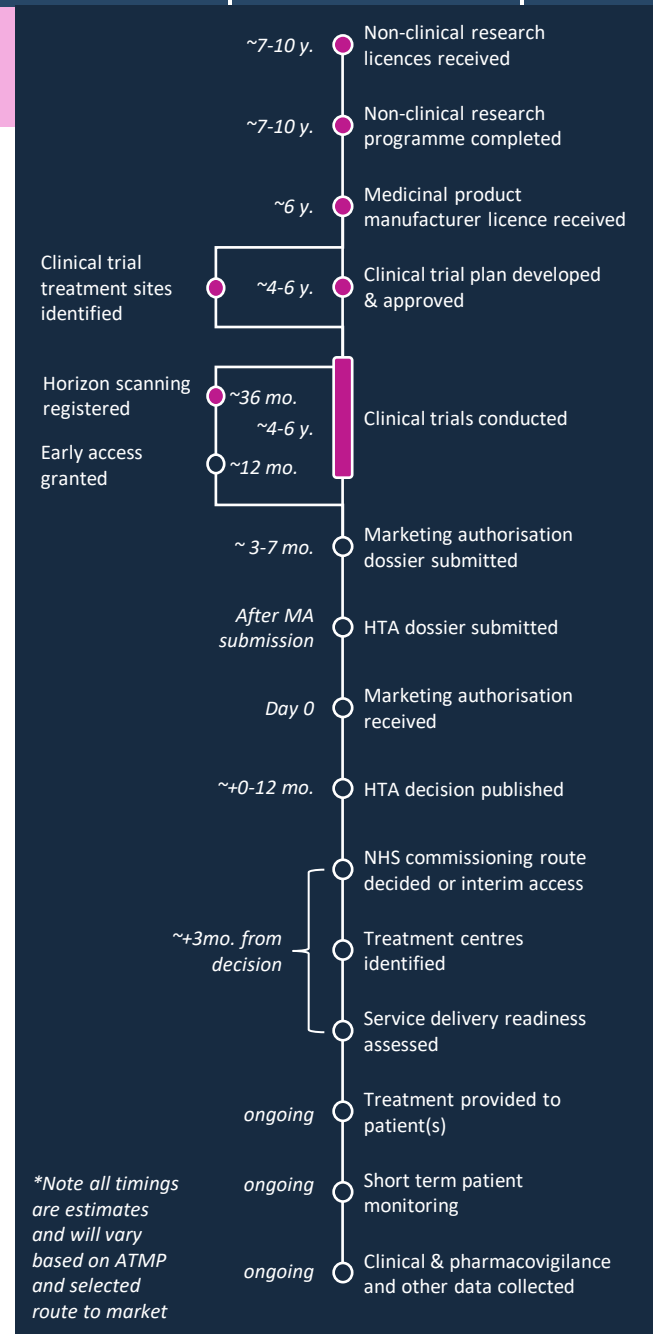
- ATMP developer
- MHRA
- FDA

Project Orbis participating countries:

- FDA (USA)
- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)
- ANVISA (Brazil)

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

## KEY TOPICS



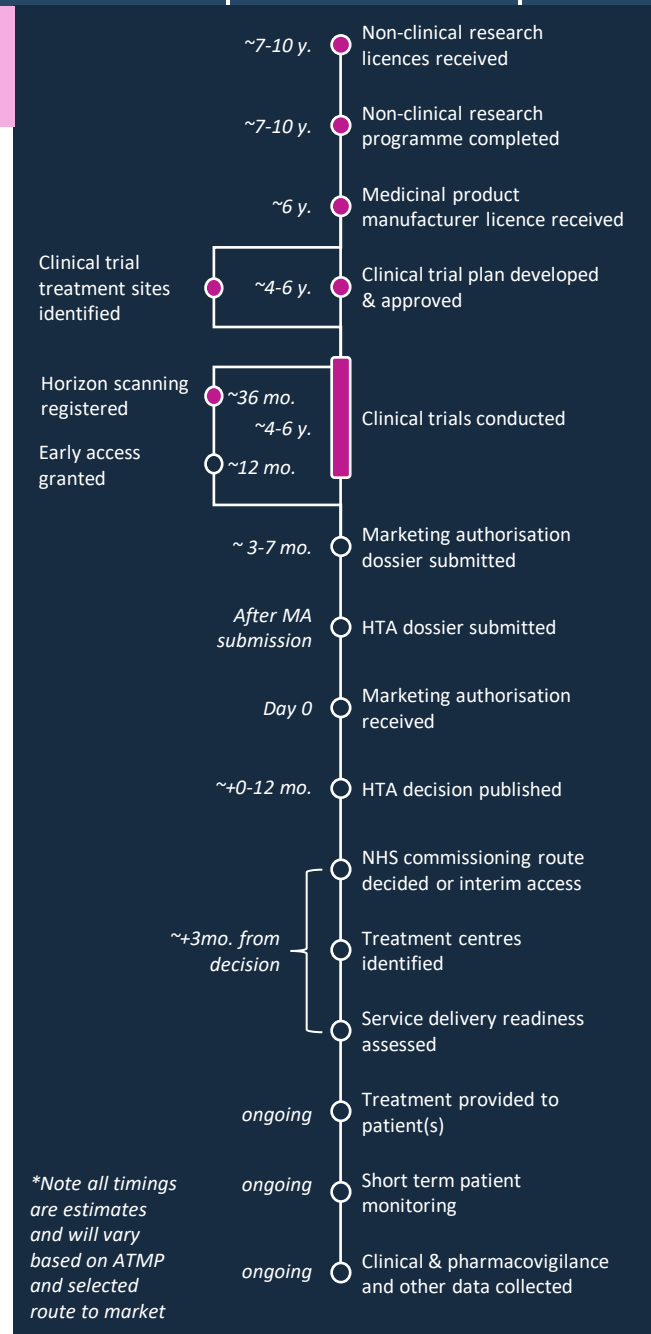
## Overview

## To-do list

## Output

- For queries relating to project Orbis, contact the MHRA at Orbis-MHRA@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

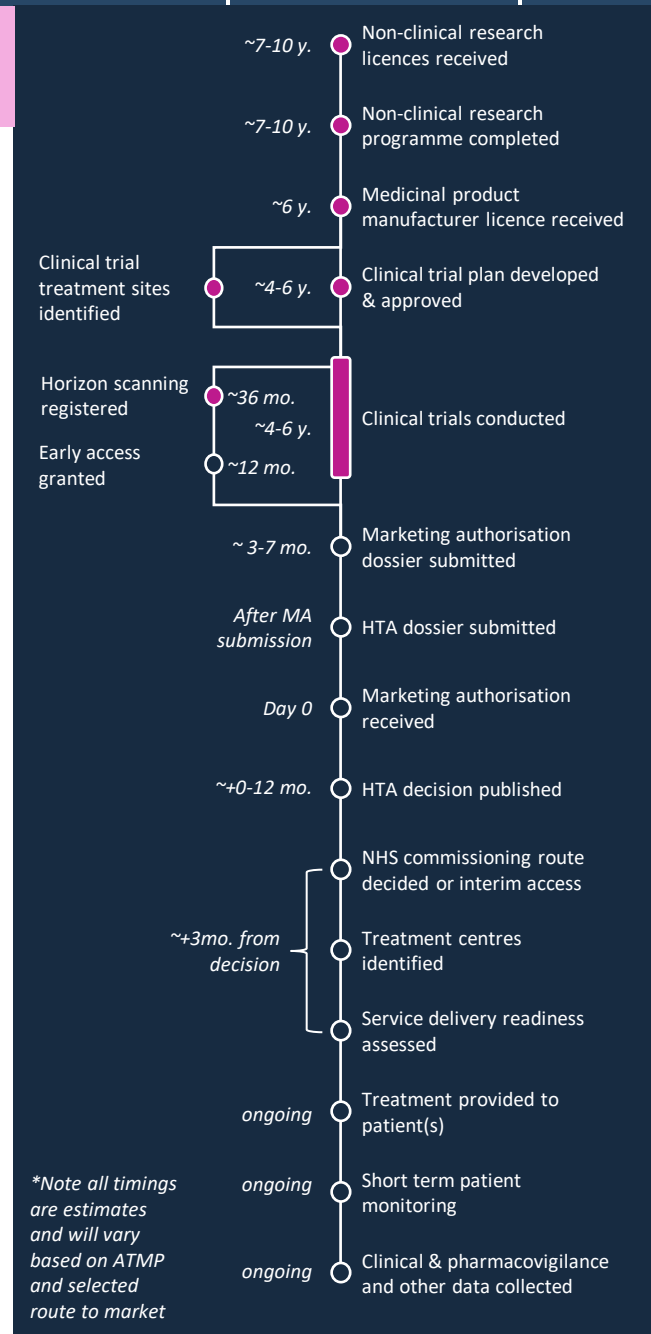


**Overview** | To-do list | Output

Developers can apply for a concurrent Marketing Authorisation submission and review in additional markets through the Access Consortium. There are a number of work sharing initiatives for different product types, so developers should review the guidance and ensure that it is relevant and applicable for their product.

Applicants for Access Consortium work sharing initiatives will still be required to submit their full Marketing Authorisation to the MHRA using their existing process, and will receive independent outcomes from participating countries. There are fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS



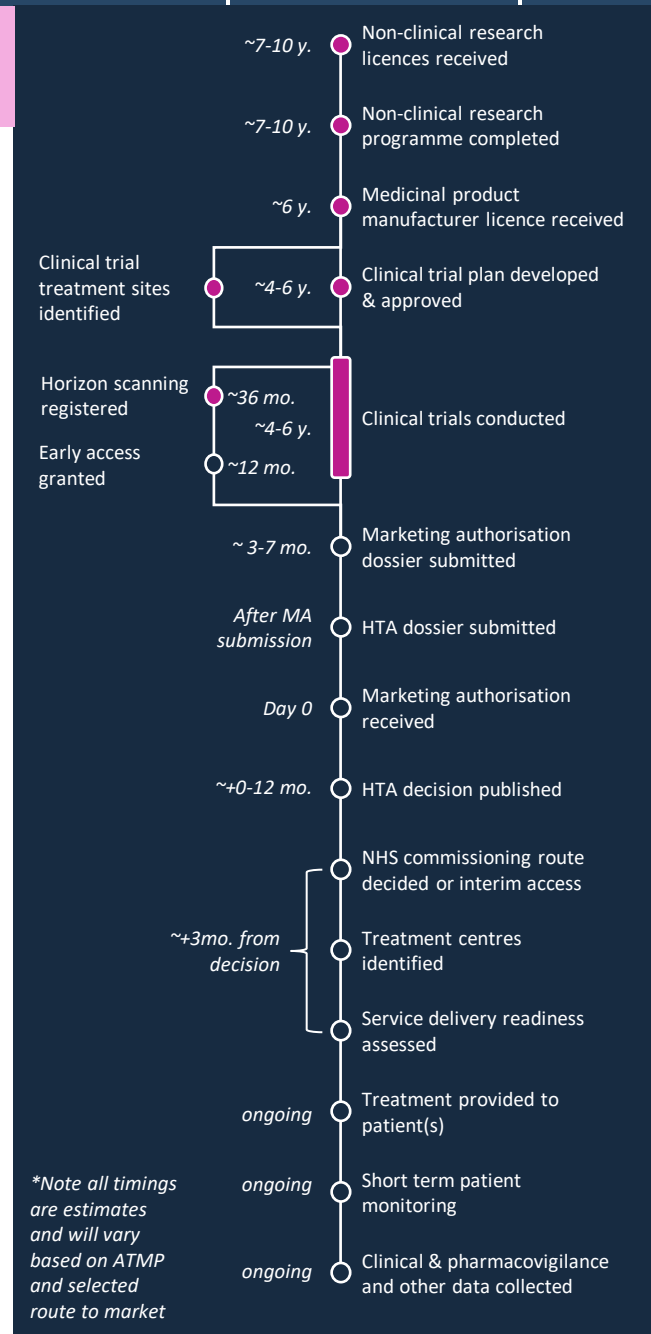
Overview | **To-do list** | Output

- Review Access Consortium guidance and determine if applicable for the product here
- Review the process for application in the New Active Substance (NAS) work sharing initiative here
- Express interest in the initiative using the expression of Interest (EOI) form available here, and submit to the MHRA (access-mhra@mhra.gov.uk) 3-6 months prior to MA submission
- Continue UK submission process along with concurrent submissions with participating countries (within 2 weeks of each other)

**When**

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips



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**2 What key regulatory steps are required to receive marketing authorisation?**

3 What programmes are available to accelerate time to market?

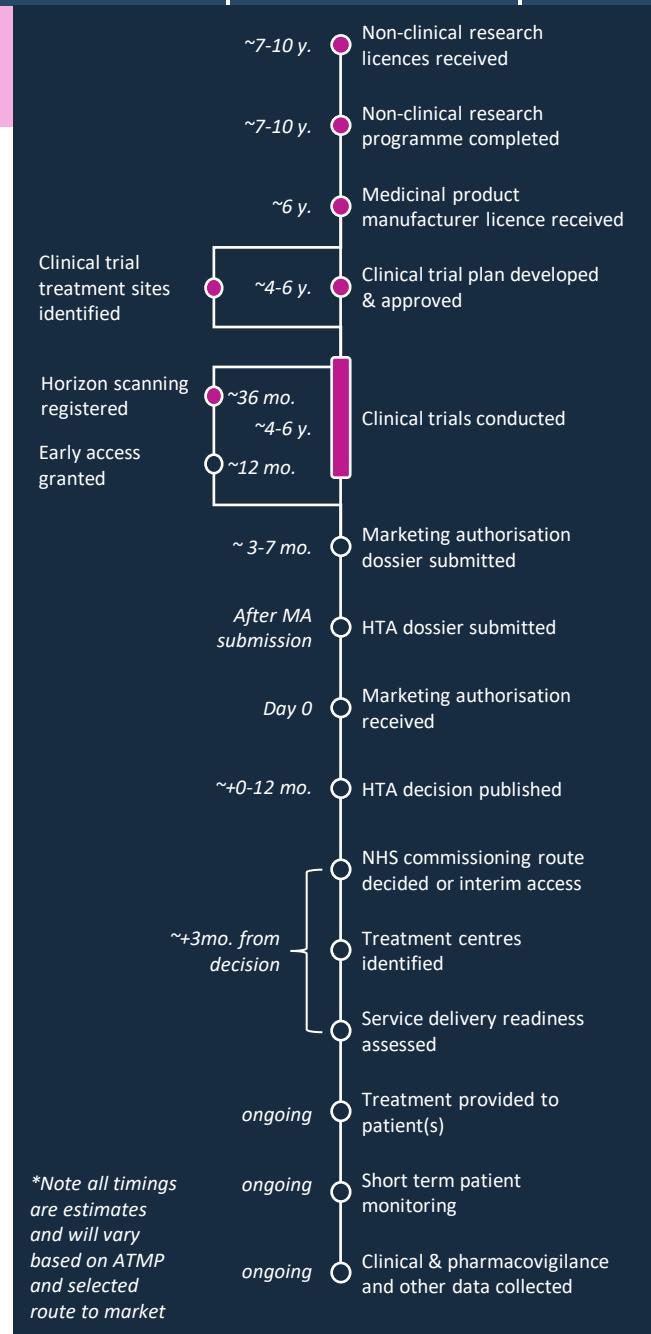
## KEY TOPICS

- Paediatric Investigational Plans approval
- Regulatory approval route selection
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**
- Marketing Authorisation submission planning
- Marketing Authorisation submission
- Post-authorisation compliance

Overview | To-do list | **Output**

- Co-ordinated review of Marketing Authorisation application
- Marketing Authorisation decision from all participating Access consortium countries

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

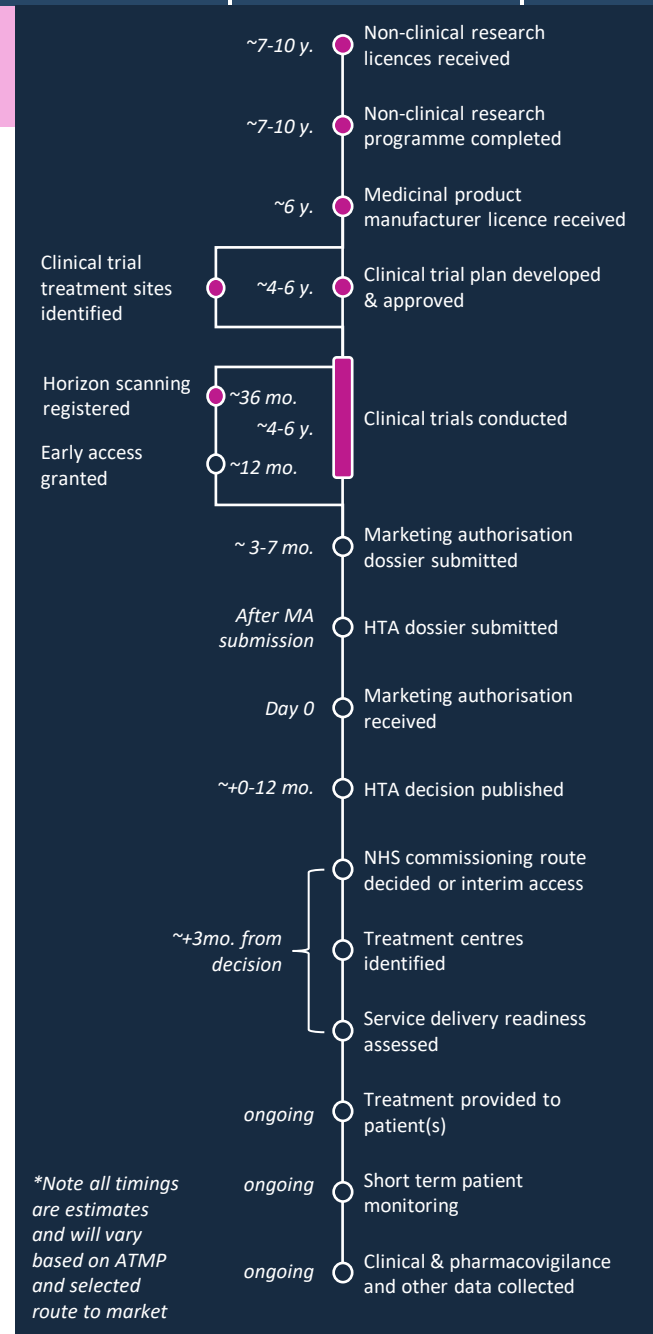
## To-do list

## Output

Marketing Authorisation submission

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

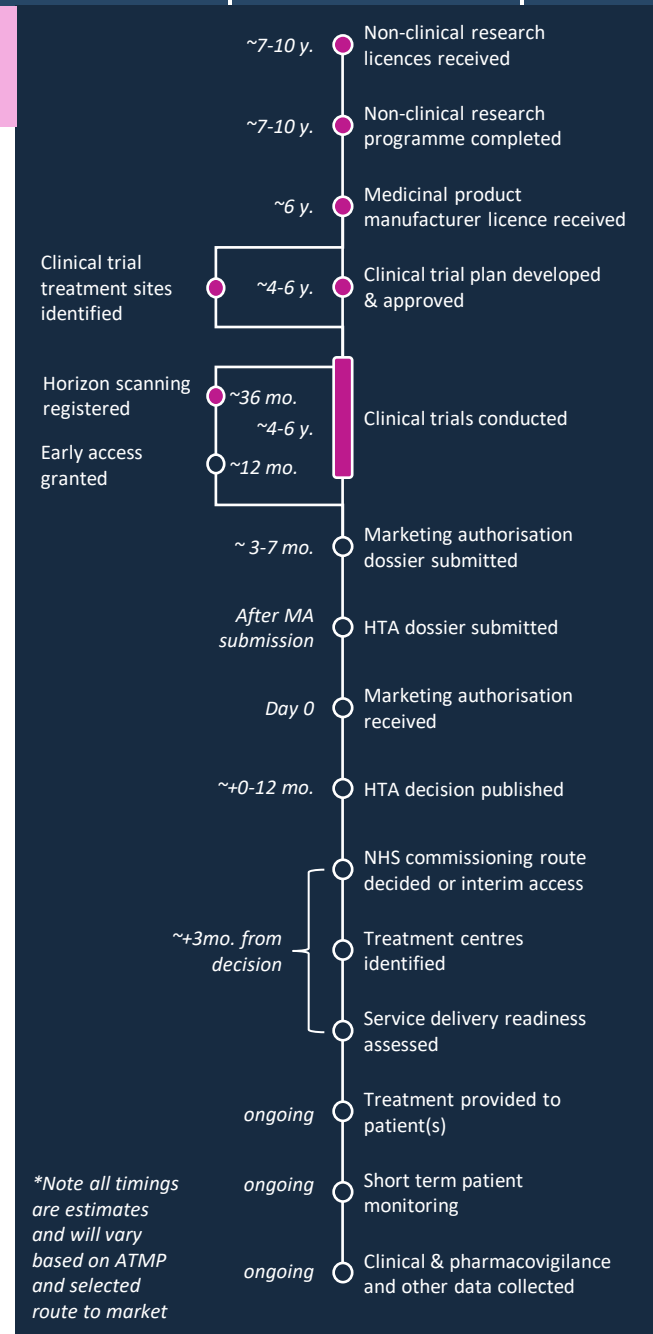
- ATMP developer
- MHRA

Access Consortium participating countries:

- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

## KEY TOPICS



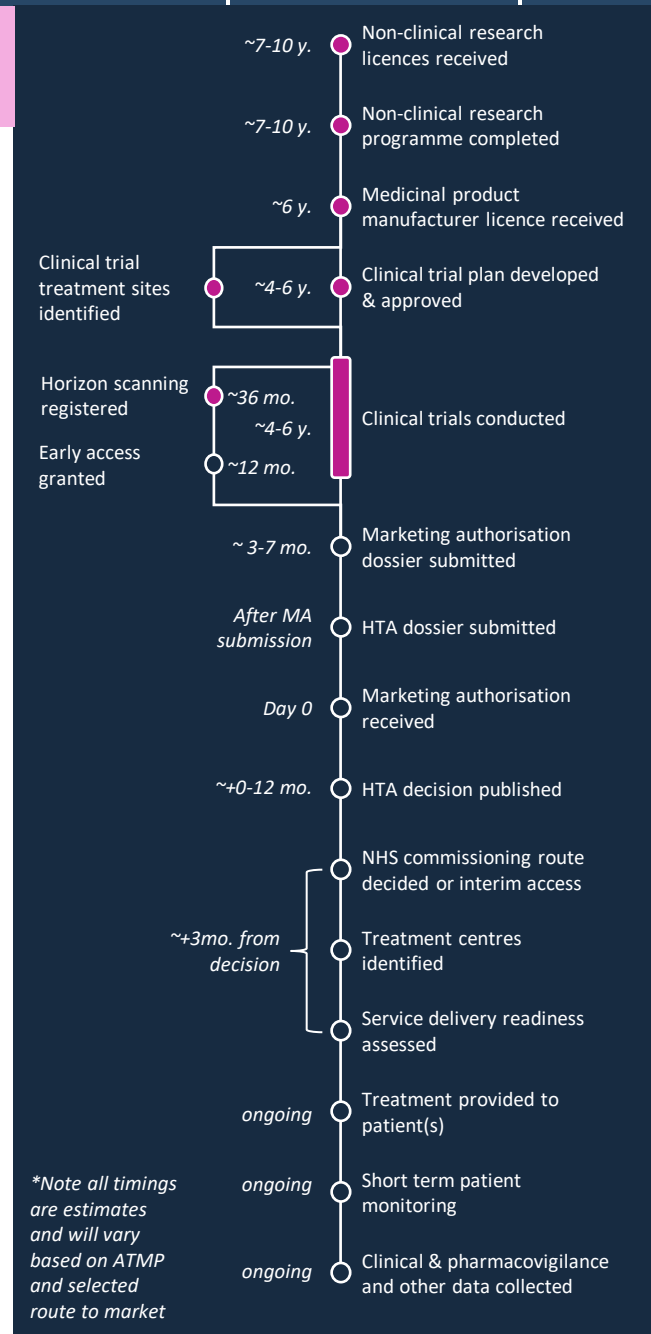
Overview

To-do list

Output

- For queries relating to Access Consortium Work Sharing Initiatives, contact the MHRA at access-mhra@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS



**Overview** | To-do list | Output

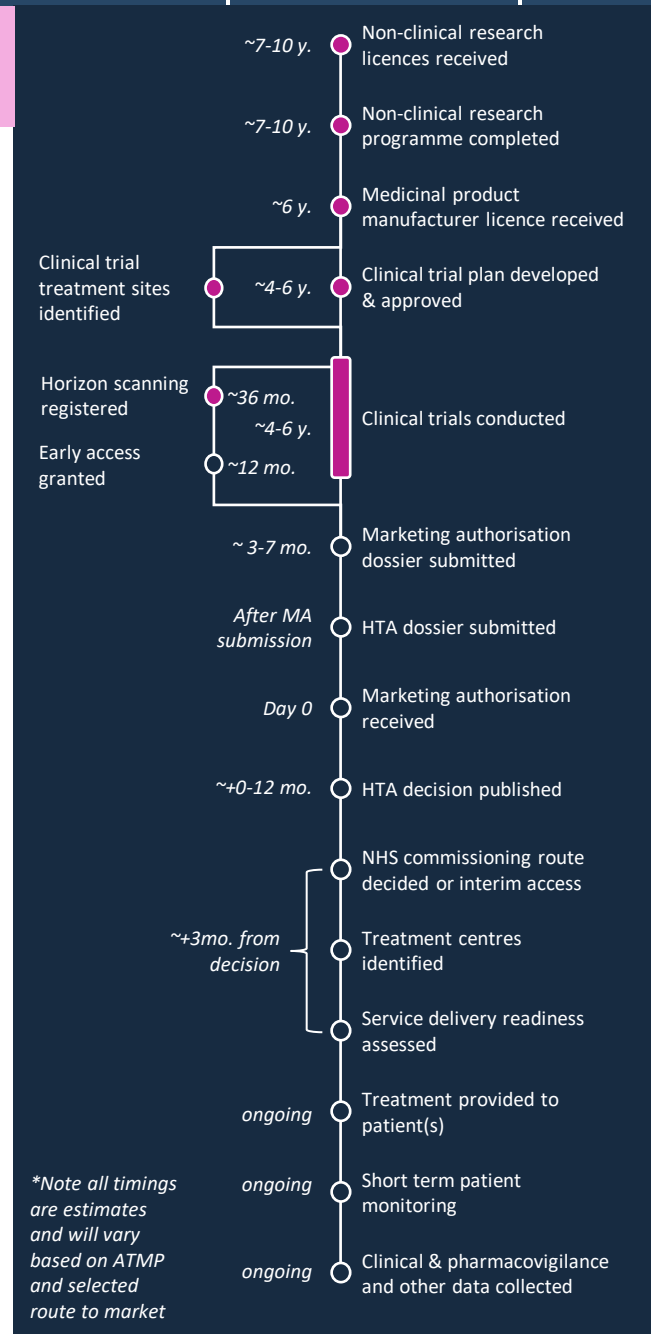
As part of Marketing Authorisation submission planning, developers should determine which Marketing Authorisation submission route they will follow and notify the MHRA.

Developers should develop a detailed submission plan and timelines. In addition to gathering all of the required documentation, developers should hold a formal meeting with the MHRA prior to submission of their application. Developers should also ensure that they have an appropriate pharmacovigilance system in place as details will need to be provided as part of the MA submission.

If the product is a combination ATMP including a medical device component, developers must ensure compliance with medical device legislation.

Developers based in Northern Ireland must ensure compliance with EMA processes and apply to the Committee for Advanced Therapies (CAT) of the EMA on the quality, safety, and efficacy of the ATMP prior to MA submission (CHMP opinion).

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS



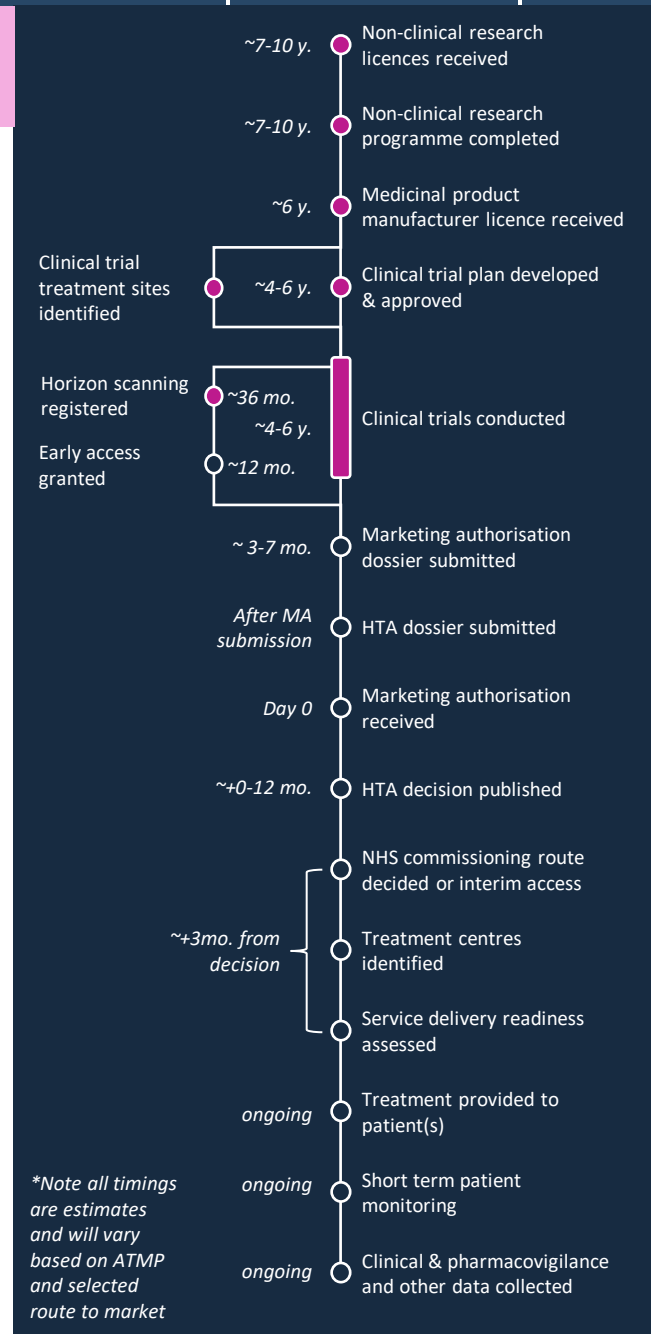
Overview | **To-do list** | Output

- Commence MHRA submission planning and notify the MHRA of the intended submission route
- Apply for a product licence number from the MHRA portal here or by emailing PLNumberAllocation@mhra.gov.uk
- If product is a combination ATMP including a medical device component, review medical device requirements here
- Review and complete pre-submission checklist here
- Hold pre-submission meeting with the MHRA
- Provide a name for the ATMP, with advice on naming here
- Create a Patient Information Leaflet (PIL) guidance here
- If required, request a meeting with the MHRA regarding the intended submission to receive regulatory advice
- Complete a UK PIP compliance check prior to Marketing Authorisation submission, guidance from MHRA here

**When**

Planning should begin prior to Marketing Authorisation submission
Pre-submission meeting should be 6 months prior to intended submission

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

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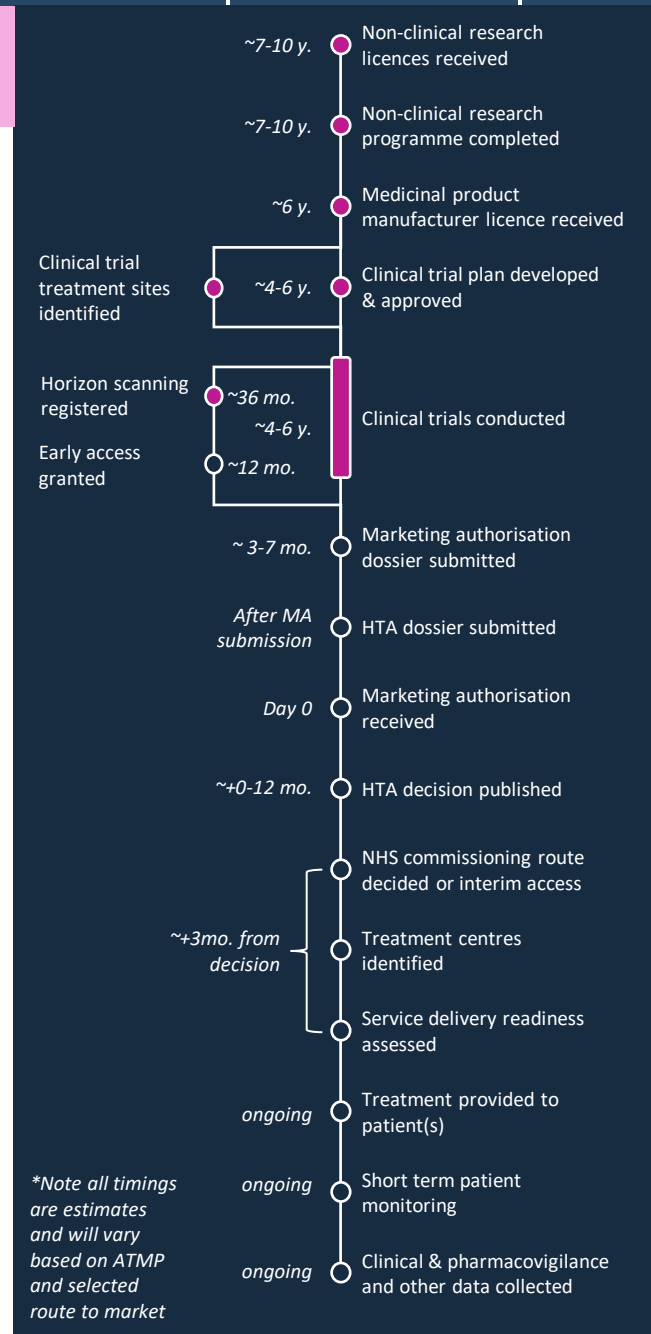
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]
- **Marketing Authorisation submission planning**
- Marketing Authorisation submission
- Post-authorisation compliance

## Overview

## To-do list

- MA submission plan
- ATMP name
- PL number
- Completed pre-submission checklist
- Pre-submission meeting with MHRA

## Output




Linked steps | Who is involved? | Best practices & tips

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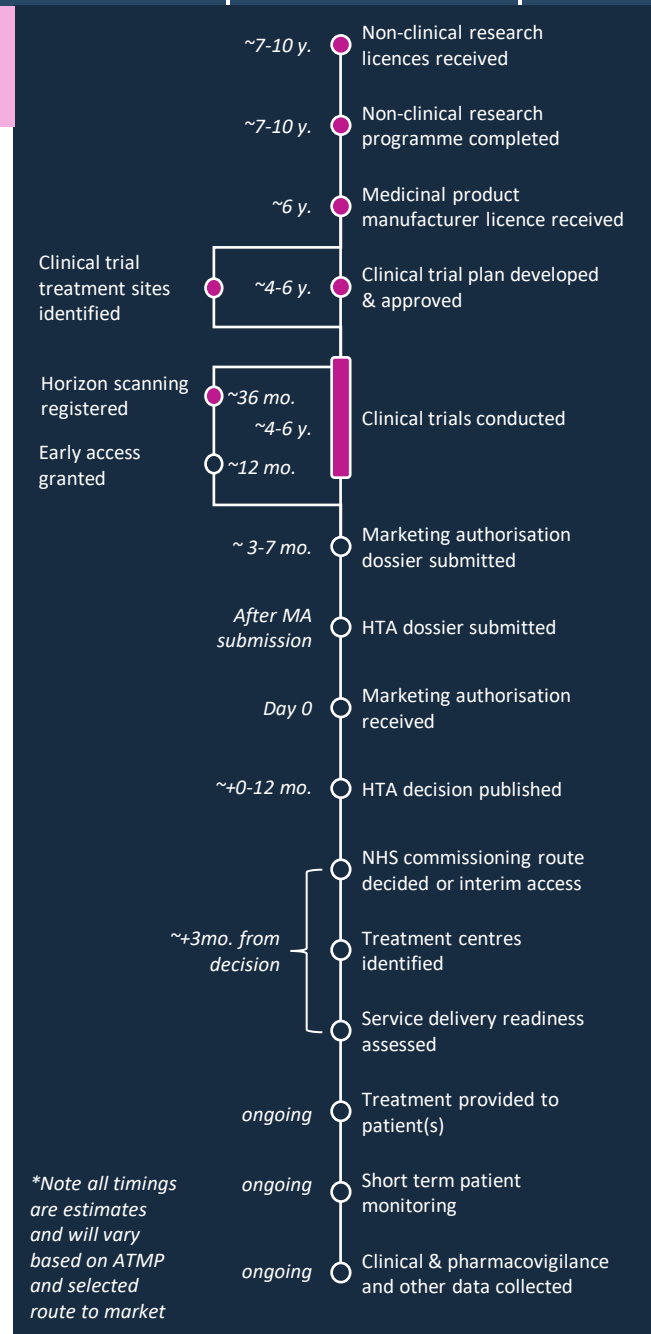
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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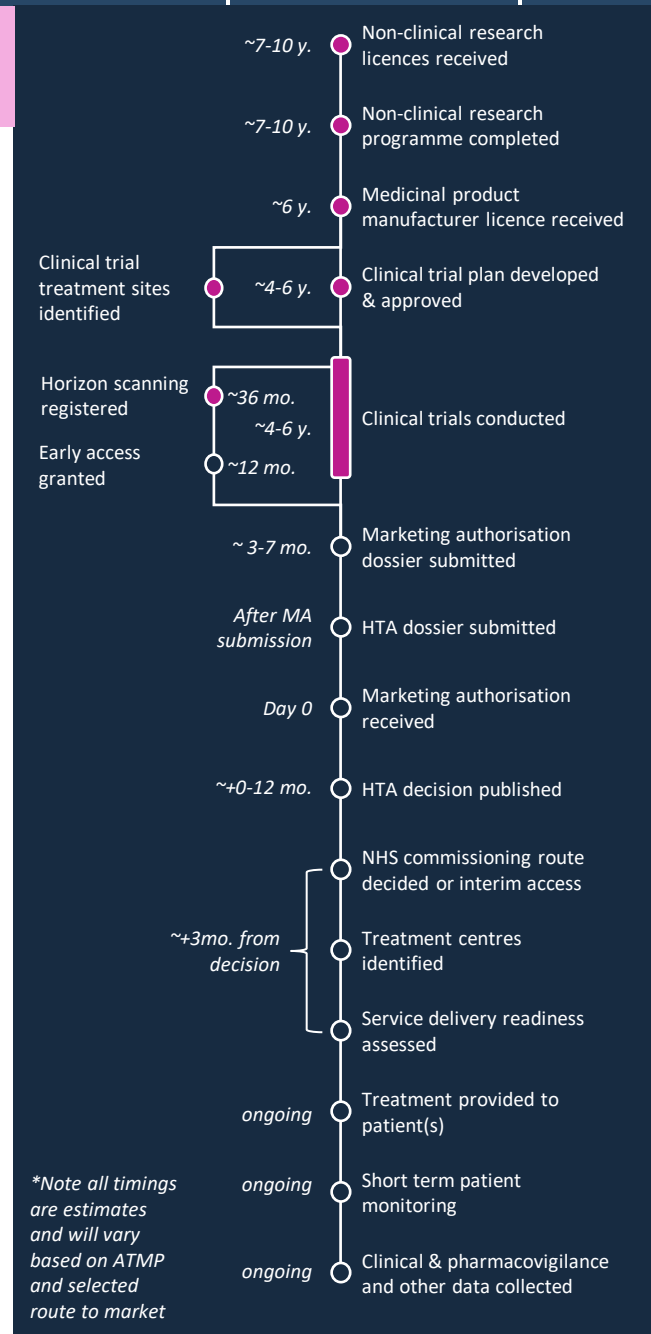
## Overview

## To-do list

## Output

- ATMP developer
- MHRA

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS



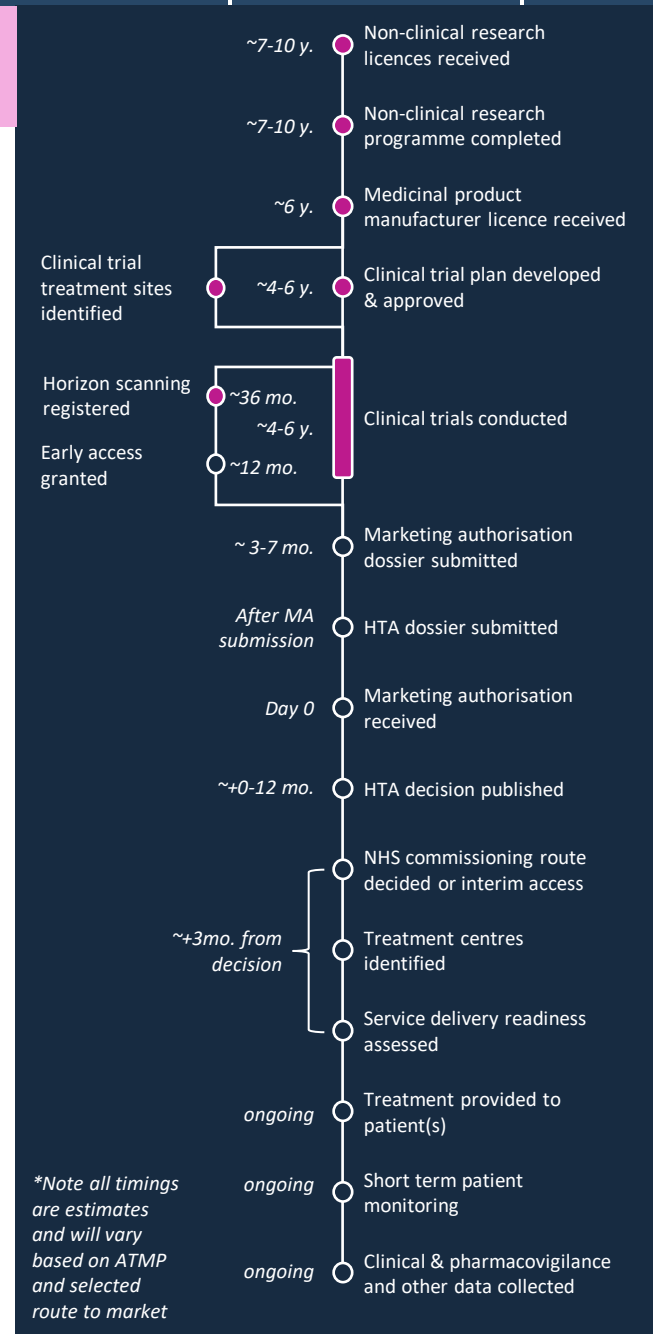
## Overview

## To-do list

## Output

- Prior to Marketing Authorisation application, developers should review and ensure that all relevant licences for their product are in place, including but not limited to; Medicinal product manufacturer's licence, HTA licence, Import/export licences and HSE GMO approval
- Developers should also make sure that any compliance reports have been completed and inspections held [if required]
- When drafting SmPC file, it is recommended to engage with the NHS at this stage to facilitate NHS implementation and prevent delays to adoption
- Contact details for the MHRA can be found here
- Developers may reach out to the Pan UK Pharmacy Working Group to ensure product is deliverable in practice and identify any potential issues for use within the NHS here

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS



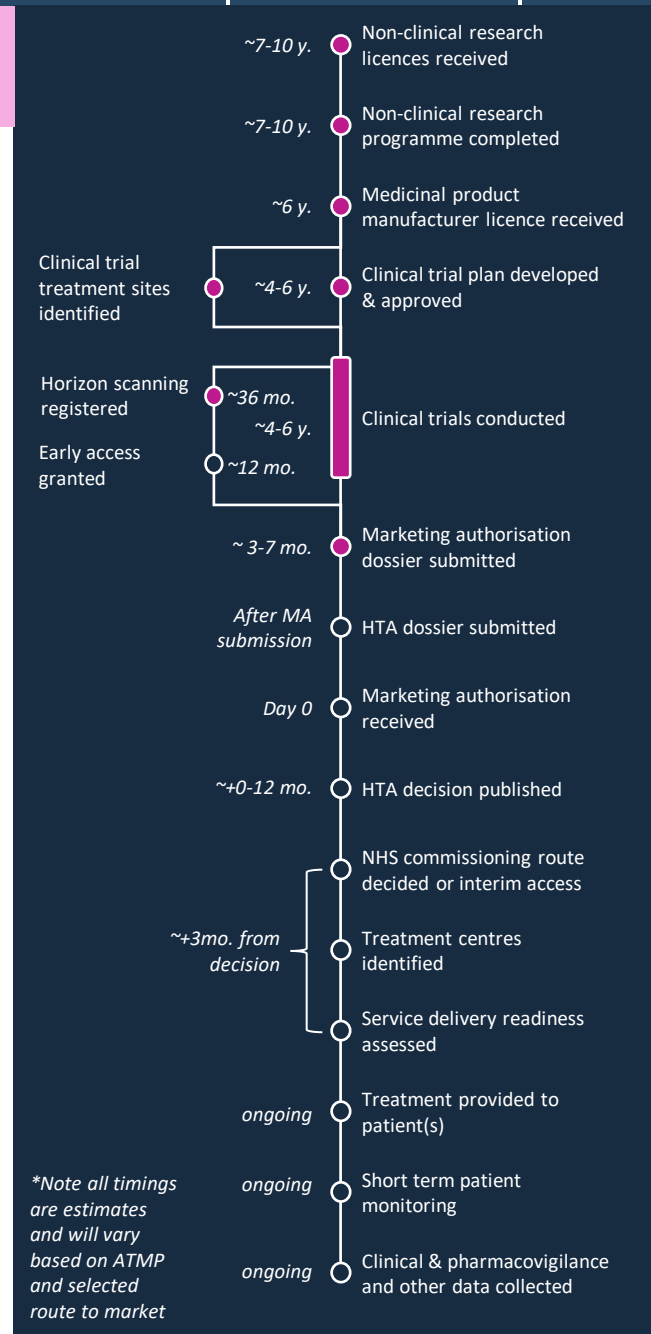
**Overview** | To-do list | Output

Developers must submit their marketing authorisation applications to the MHRA through the MHRA submissions portal, using the electronic Common Technical Document (eCTD). For developers including an application for Northern Ireland, the application must comply with EU requirements.

For developers of ATMPs that meet orphan designation requirements, application for Orphan designation must be submitted at the time of UK MA submission. For developers of ATMPs which already hold an Orphan designation from the EU, they must apply for a GB Orphan designation, rather than UK-wide.

There are fees involved for Marketing Authorisation applications.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

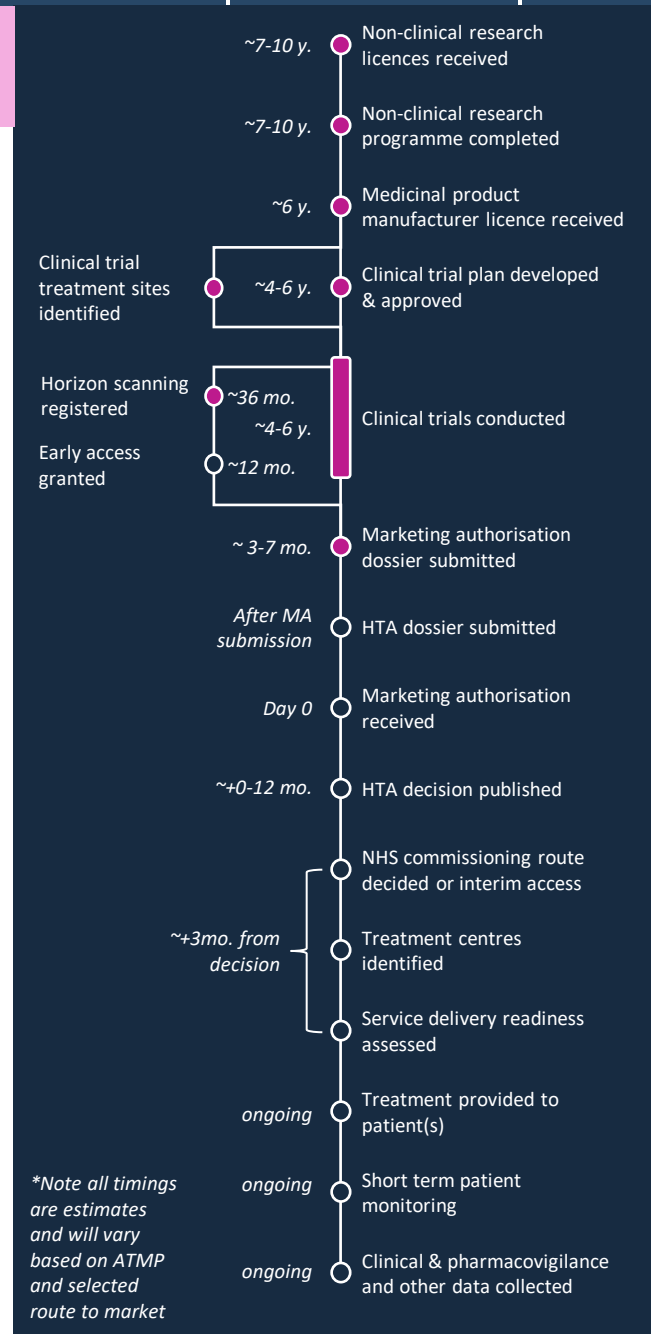


Overview | **To-do list** | Output

- Review guidance on MA submission here
- Complete MA application through the eCTD here which must be submitted through the MHRA submissions portal
    - Review process and register for access to the MHRA submissions portal here
- Review guidance for Orphan Designation in the UK here
- If applicable, apply for Orphan Designation at the time of submitting Marketing Authorisation Application through the application form here
- If the application includes Northern Ireland, then it must comply with EU requirements, outlined here

**When**
Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips

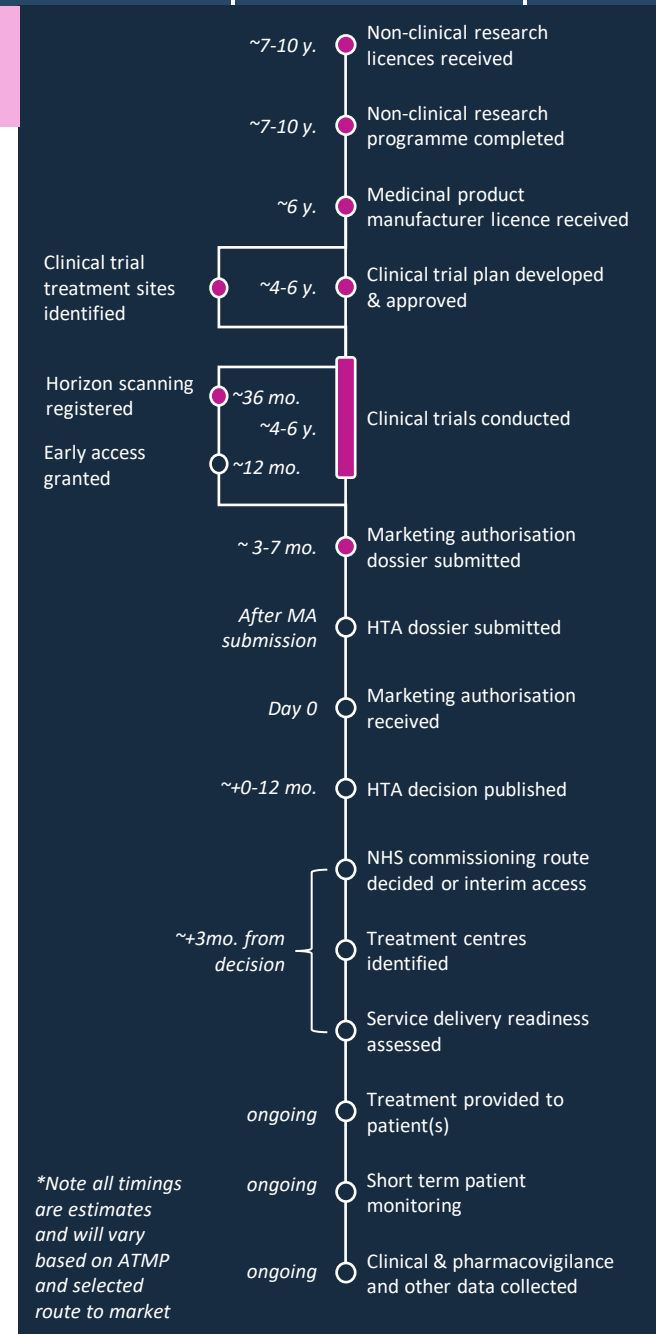


## KEY TOPICS



Overview | To-do list | **Output**

- Submitted Marketing Authorisation application
- Marketing Authorisation decision:
  - MA approval
  - Conditional or exceptional circumstance MA (guidance here)
  - MA rejection and option to appeal or re-submit application with requisite amendments
- Orphan designation decision [if applicable]
  - If successful, product will be listed on the orphan register and receive a market exclusivity period of 10 years (12 years for paediatric)



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- Marketing Authorisation submission planning
- **Marketing Authorisation submission**
- Post-authorisation compliance

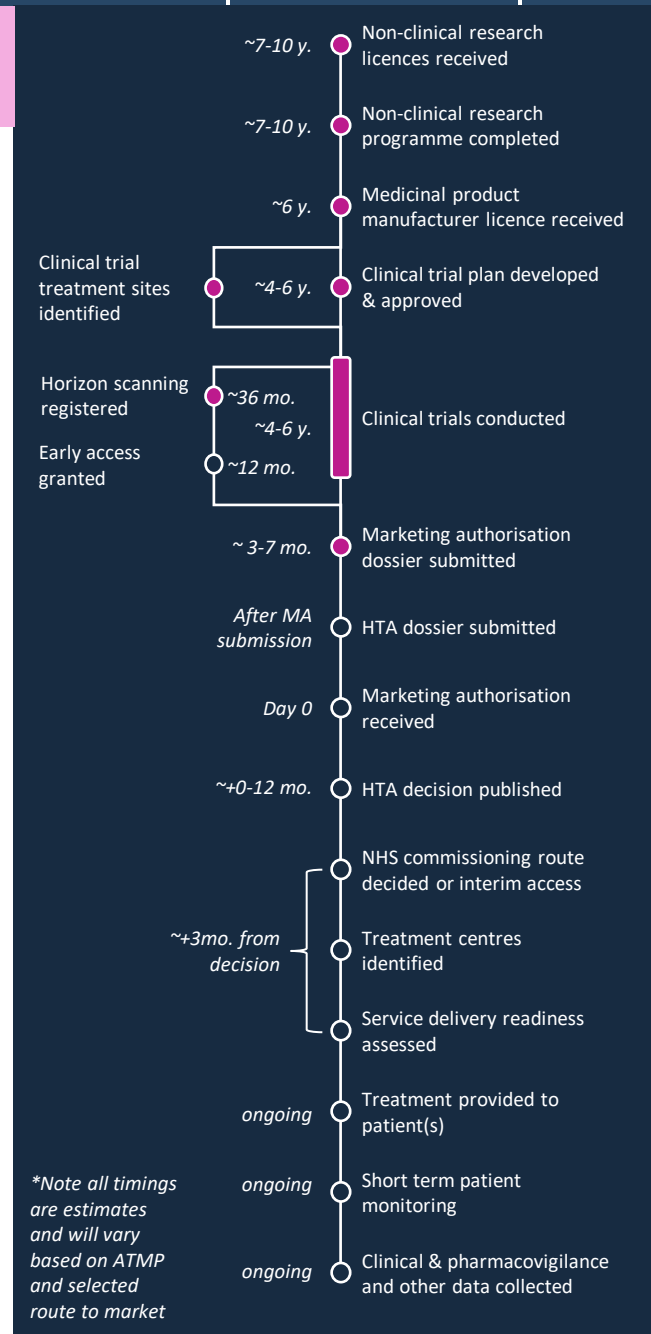
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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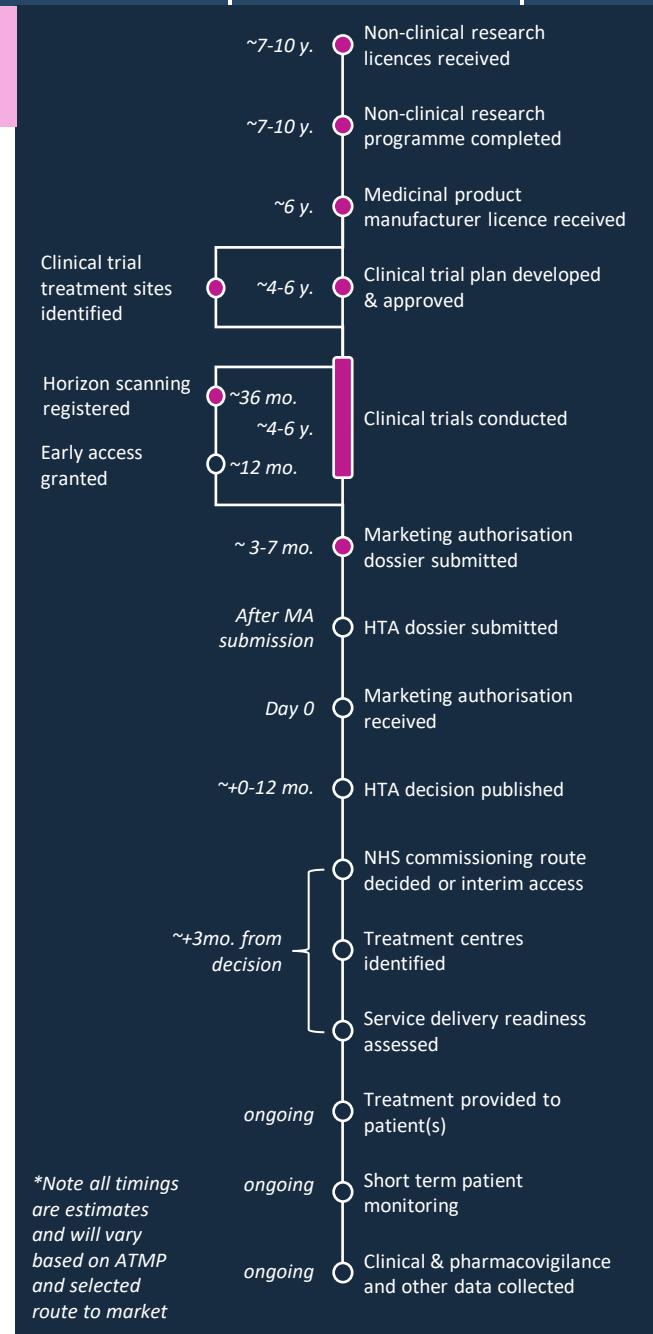
## Overview

- ATMP developer
- MHRA

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



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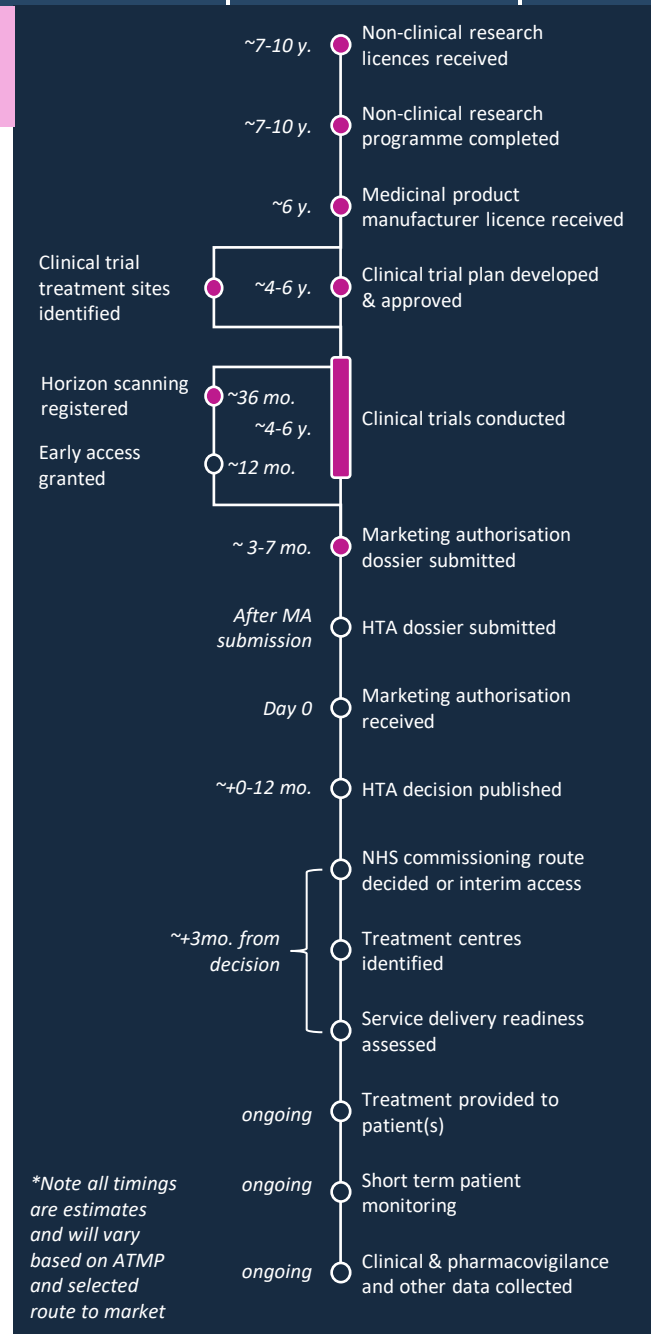
## Overview

## To-do list

## Output

- Companies should be prepared to receive questions during assessment procedure
- Contact details for the MHRA can be found here

**Linked steps** **Who is involved?** **Best practices & tips**



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- Marketing Authorisation submission
- **Post-authorisation compliance**

**Overview** | To-do list | Output

For successful marketing authorisation (MA) applications, MA holders should review any MA conditions to ensure compliance with any Post-Authorisation obligations and ongoing pharmacovigilance procedures [if applicable].

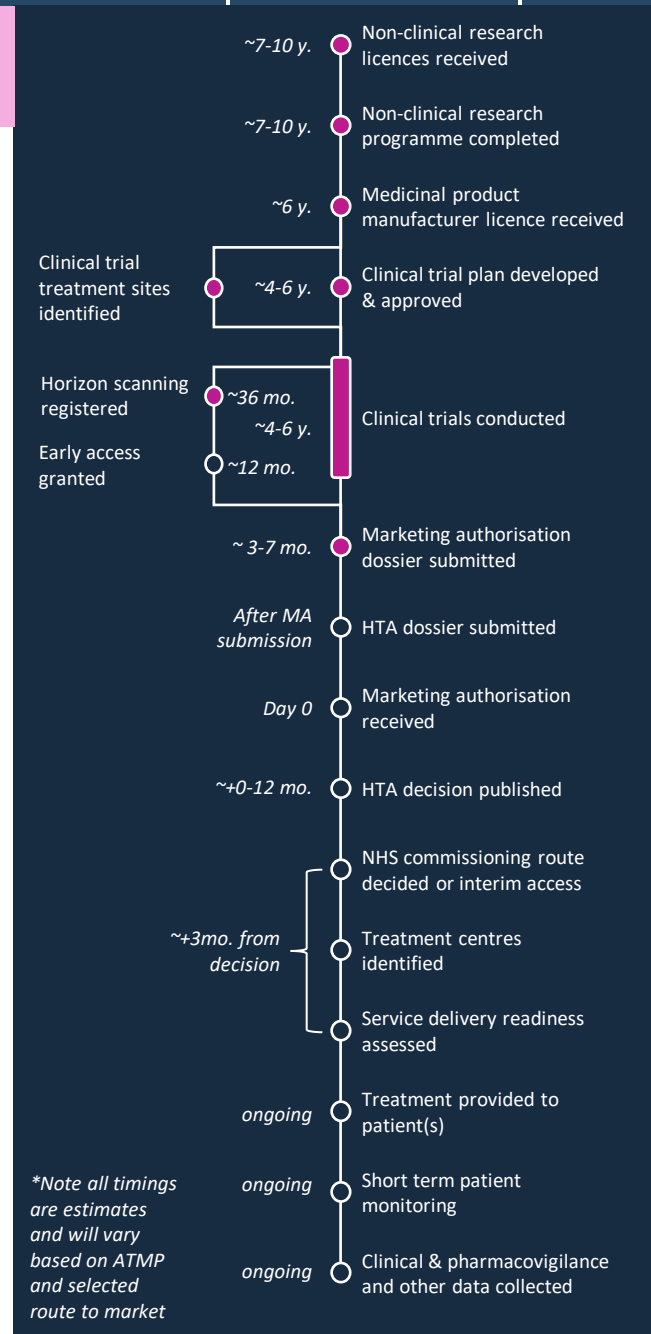
These include but may not be limited to:

- UK and non-UK Individual Case Safety Reports (ICSRs)
- Periodic Safety Update Reports (PSURs)
- Risk Management Plans (RMPs)
- Post-Authorisation Safety Studies (PASS) protocols and final study reports
- Other conditions of Marketing Authorisation
- Long-term follow up studies

Marketing Authorisations are typically granted for 5 years but this may vary, the renewal date will be provided in the MA approval.

Developers should review the process for renewing, amending or transferring their manufacturing authorisation if applicable. There are fees involved for these services.

**Linked steps** | **Who is involved?** | **Best practices & tips**



## KEY TOPICS



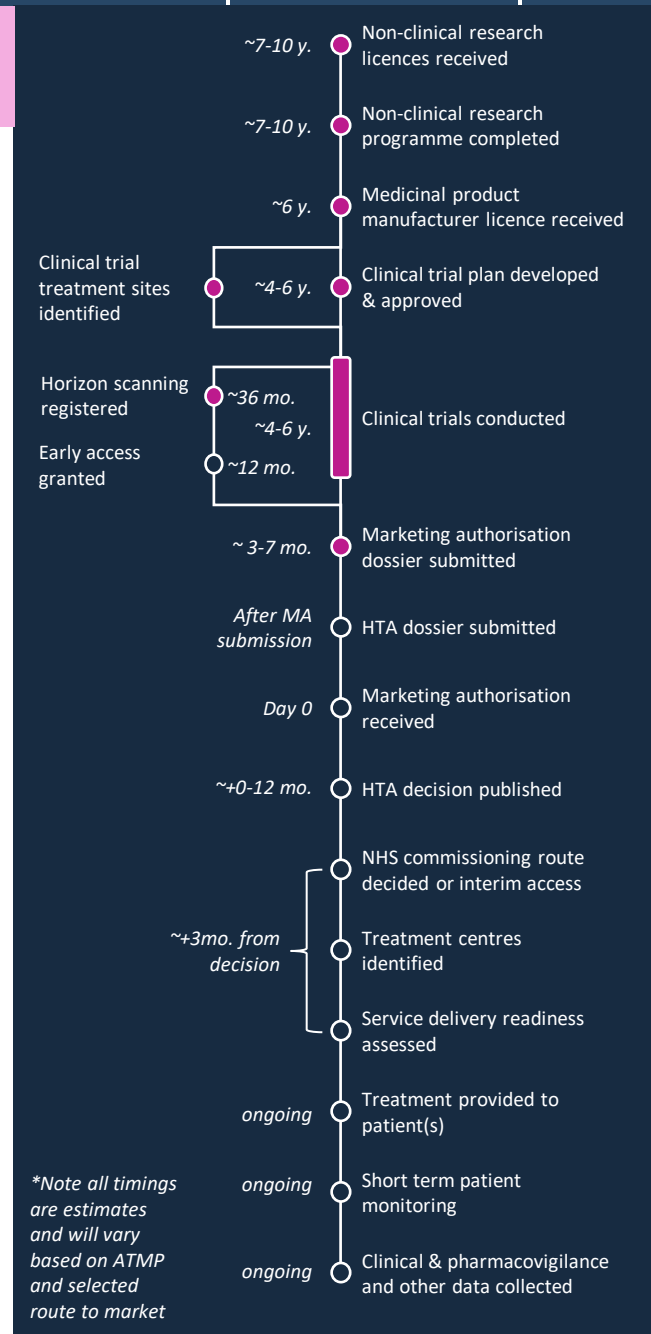
Overview | **To-do list** | Output

- Review any Marketing Authorisation conditions [if applicable] to ensure compliance with any Post-Authorisation obligations
- Review full guidance from MHRA on pharmacovigilance procedures here
    - EMA guidance on Good Pharmacovigilance Practices (GPvP) can be found here with MHRA guidance on their application in the UK here
- Guidance on renewing Marketing Authorisations can be found here
- Guidance on making a variation to a Marketing Authorisation can be found here
- Guidance on transferring ownership of a Marketing Authorisation can be found here
- Guidance on reporting to the MHRA yellow card scheme can be found here

**When**

After Marketing Authorisation submission

**Linked steps** | **Who is involved?** | **Best practices & tips**



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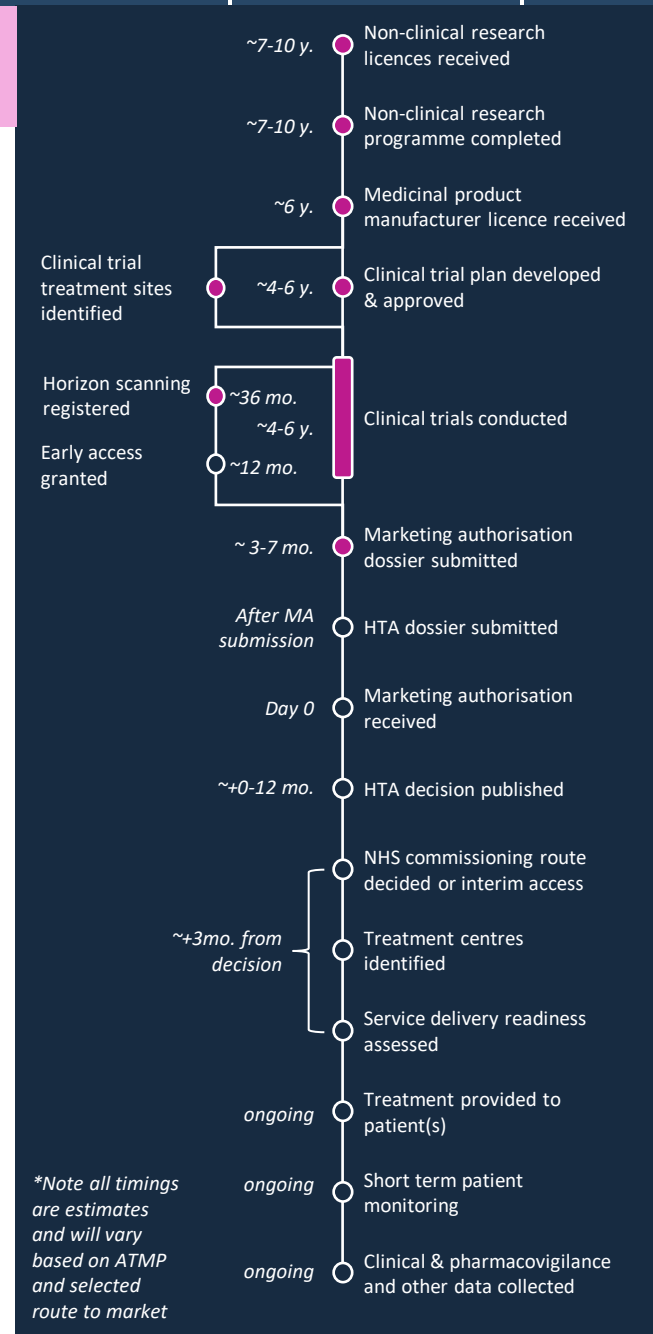
- **Post-authorisation compliance**

Overview | To-do list | **Output**

- Completed relevant pharmacovigilant procedures
- Marketing Authorisation variation/renewal/transfer of ownership

**Linked steps** | **Who is involved?** | **Best practices & tips**



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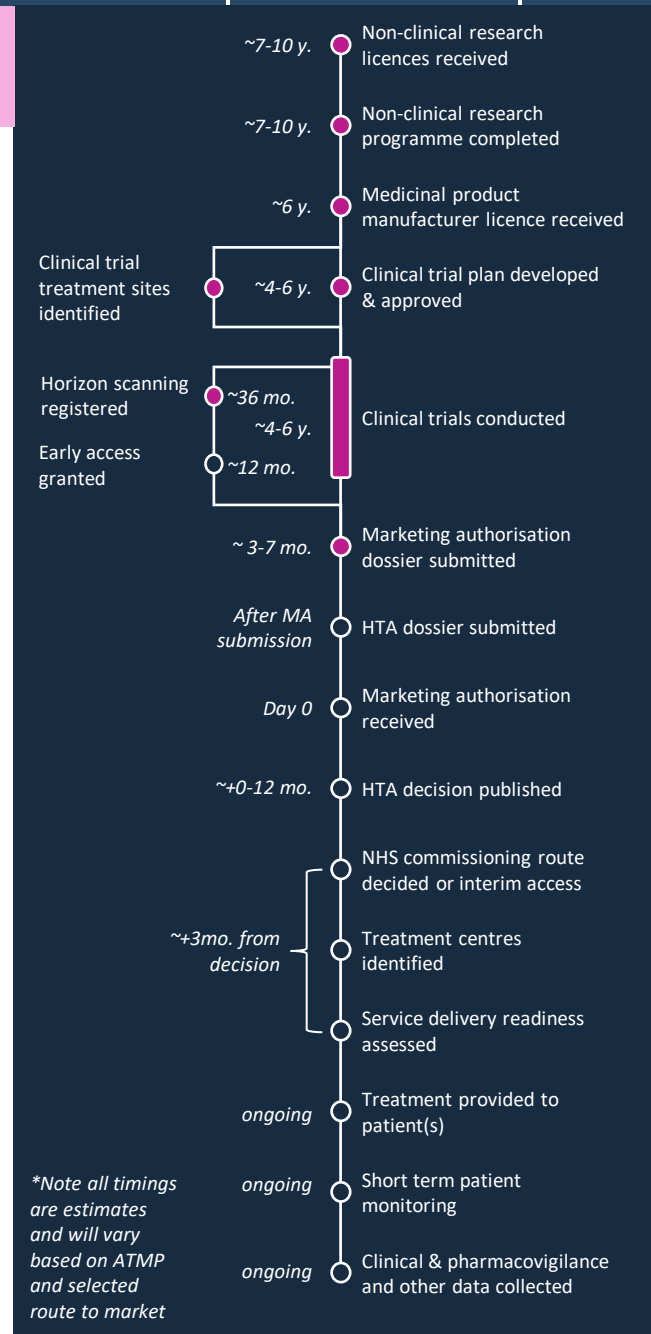
Overview

To-do list

Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- Marketing Authorisation submission
- **Post-authorisation compliance**

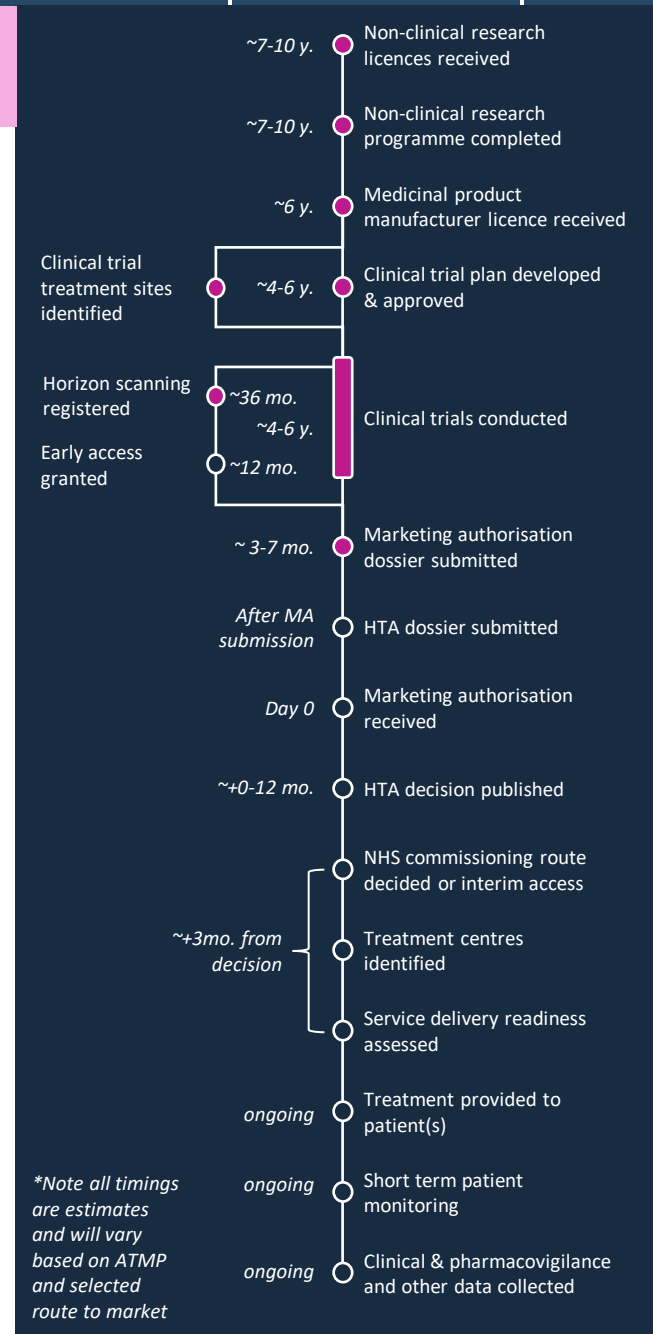
## Overview

- ATMP developer
- MHRA

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



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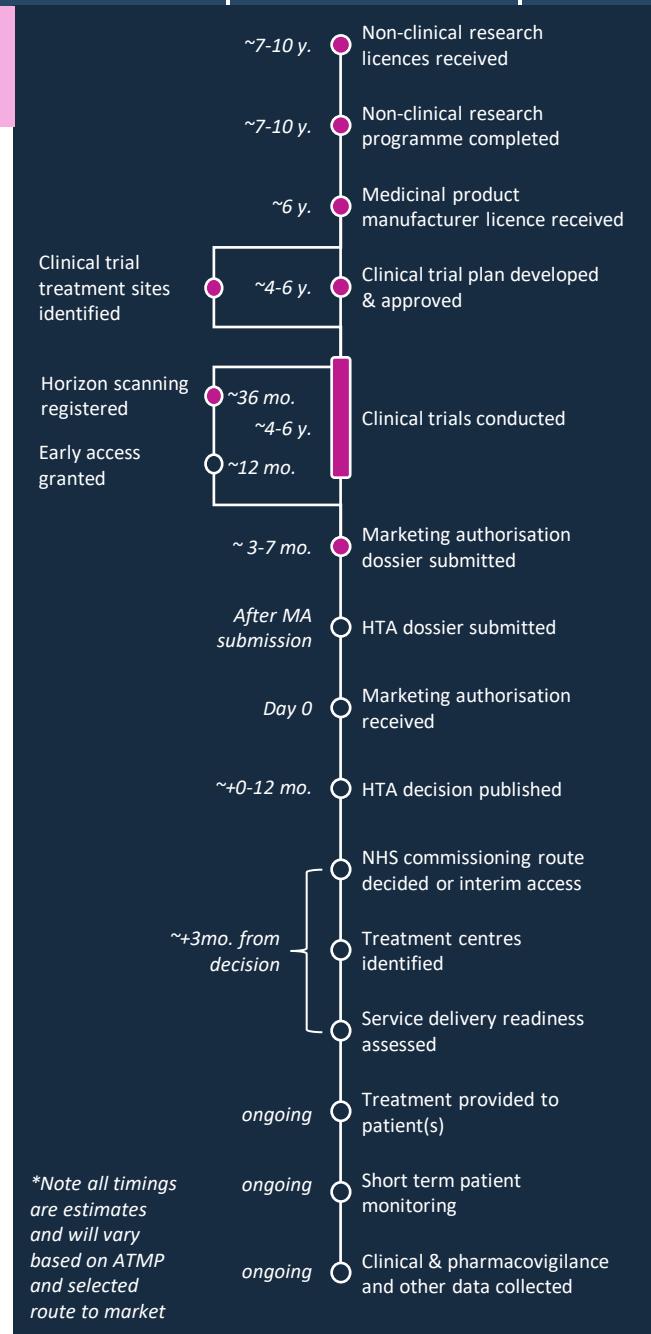
Overview | To-do list | Output

- Contact details for the MHRA can be found here

**Linked steps** | **Who is involved?** | **Best practices & tips**



## KEY TOPICS



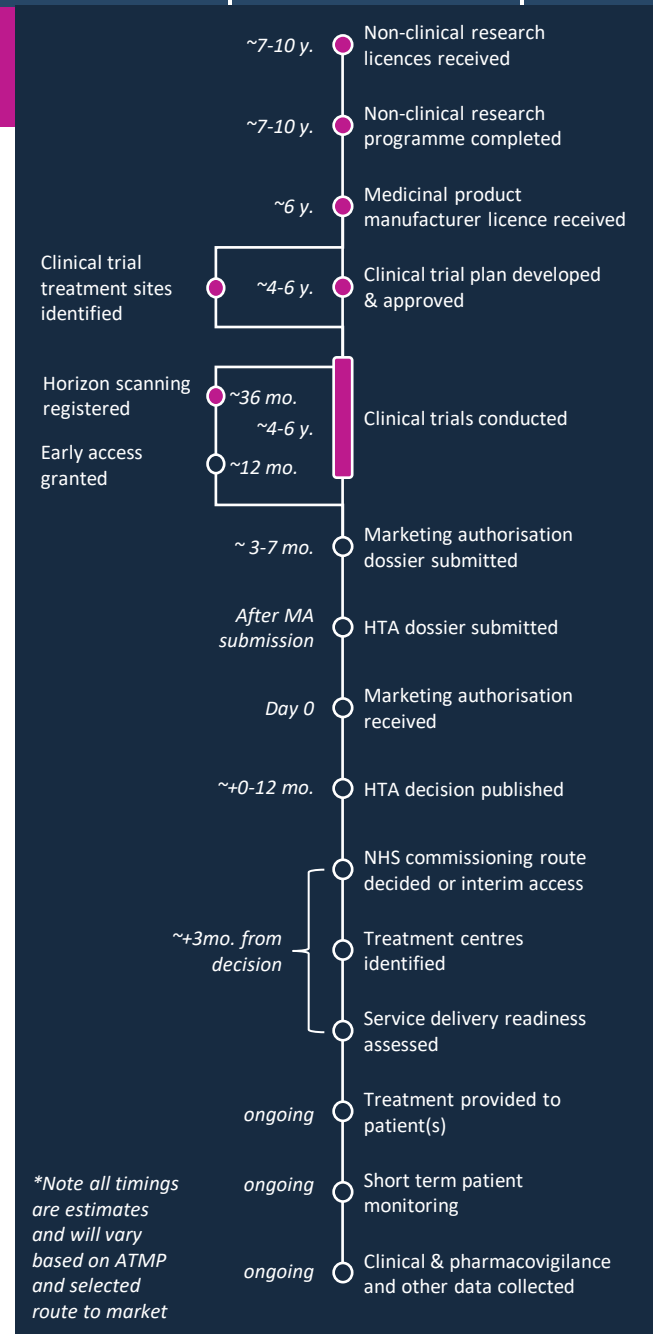
**Overview** | To-do list | Output

The Innovative Licensing and Access Pathway (ILAP) aims to accelerate the time to market, facilitating patient access to medicines. ILAP provides applicants with access to a toolkit to support all stages of the design, development and approvals process, along with opportunities for enhanced regulatory and other stakeholder input.

Developers should review the guidance on ILAP, and, if applicable, apply to the MHRA for Innovation Passport designation. Developers will then be required to attend a meeting with the MHRA regarding their application and receive an outcome decision. There are fees involved for these services.

If successful, Innovation Passport Holders are eligible to receive a customised Target Development Profile roadmap* (TDP) to guide ongoing development, along with early engagement and ongoing advice with the MHRA, NICE and the SMC.

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

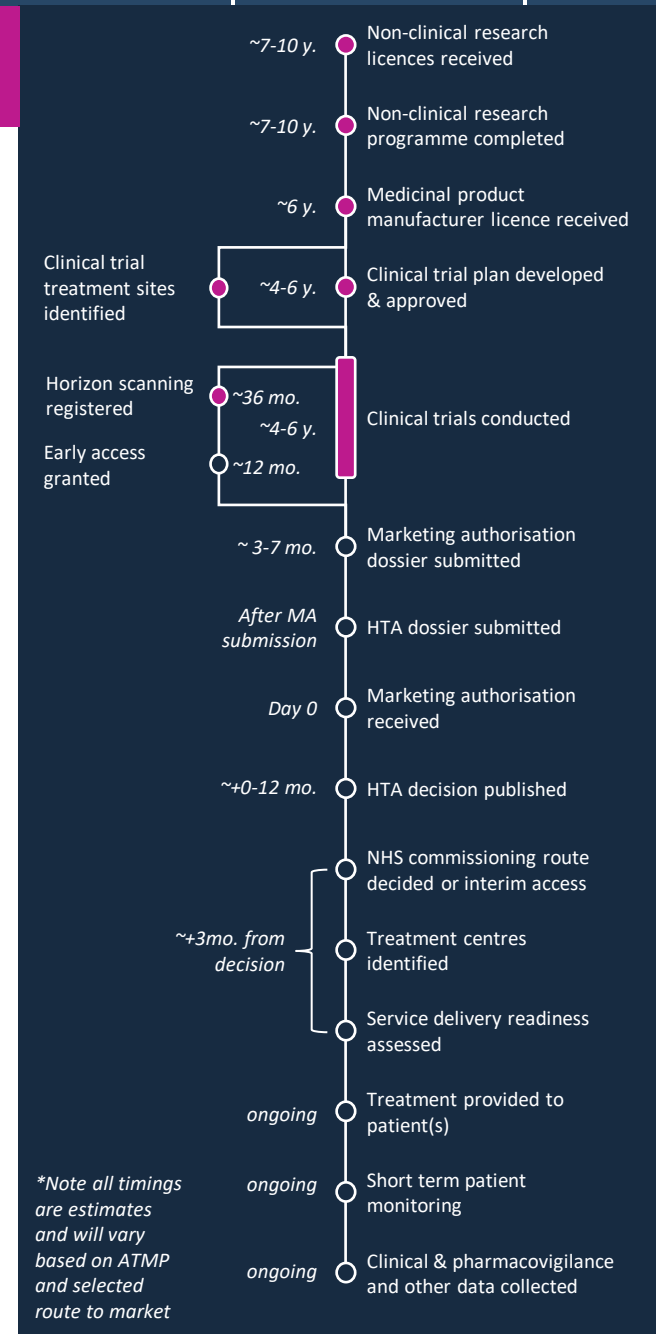
Overview | **To-do list** | Output

- Review the MHRA guidance on the ILAP process here
- Complete the MHRA Innovation Passport application form here
- Meet with the MHRA to discuss how the ATMP meets the application criteria (within 4-6 weeks of the application submission) viewed here
- Receive innovation passport outcome (within 4 weeks of the meeting)
- Submit Target Development Profile (TDP) submission form to the MHRA here
- Review the TDP toolkit here
- Hold TDP meeting with all ILAP partners following positive Innovation Passport outcome

**When**

Developers can apply for ILAP at any point prior to marketing authorisation approval

**Linked steps** | **Who is involved?** | **Best practices & tips**



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

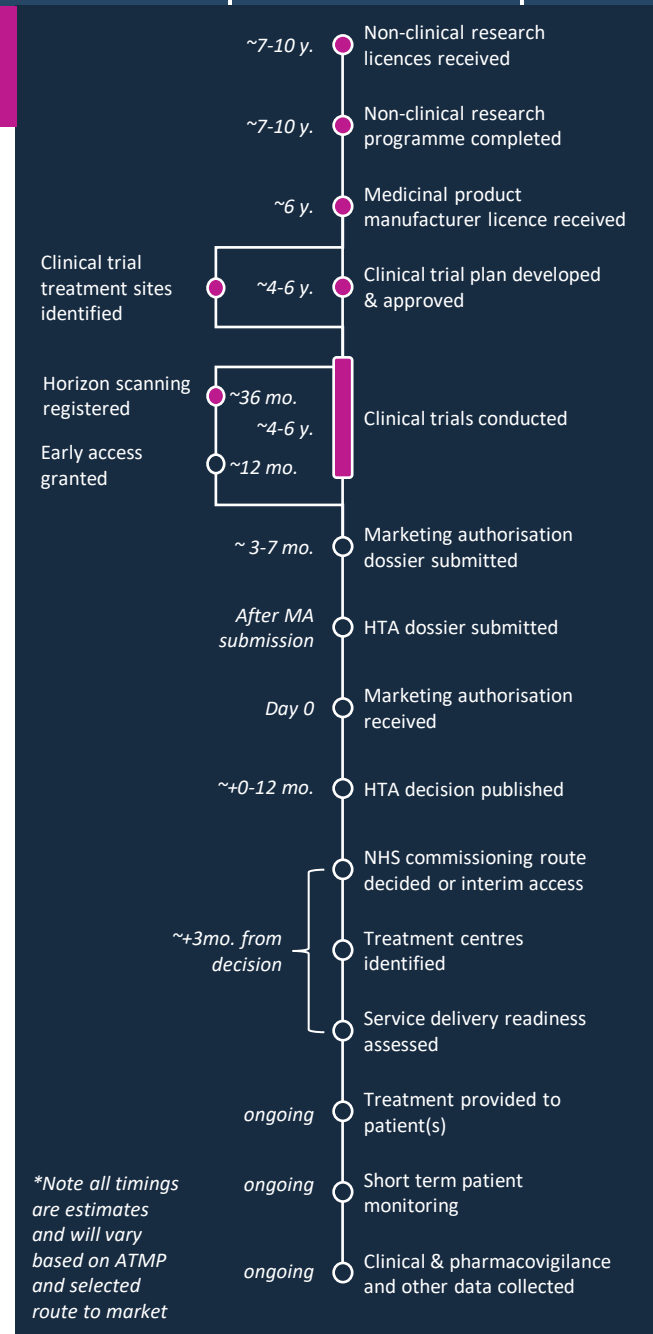
- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

Overview | To-do list | **Output**

- Innovation Passport designation
- Customised Target Development Profile roadmap*
- Ongoing engagement and support from the MHRA, NICE (and SMC and AWTTC as applicable)

* The TDP is available for all developers who are awarded an Innovation passport, however for companies at a later stage of development it may not be relevant

Linked steps | Who is involved? | Best practices & tips



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2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

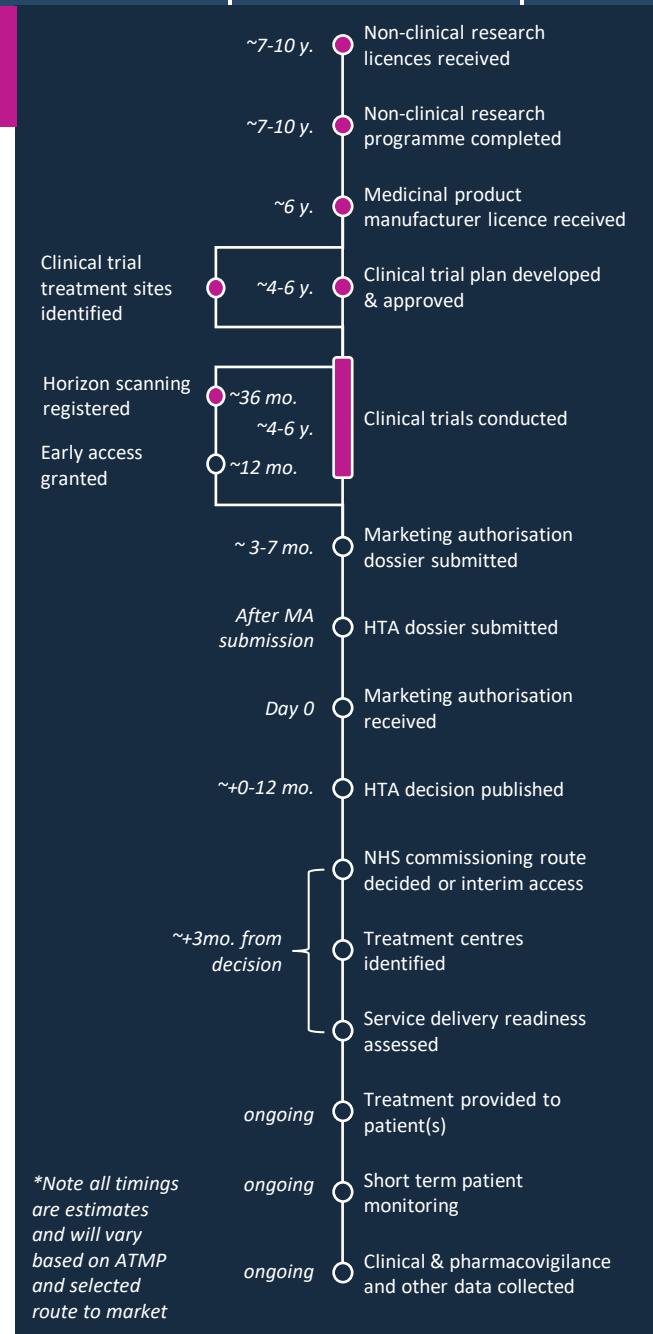
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

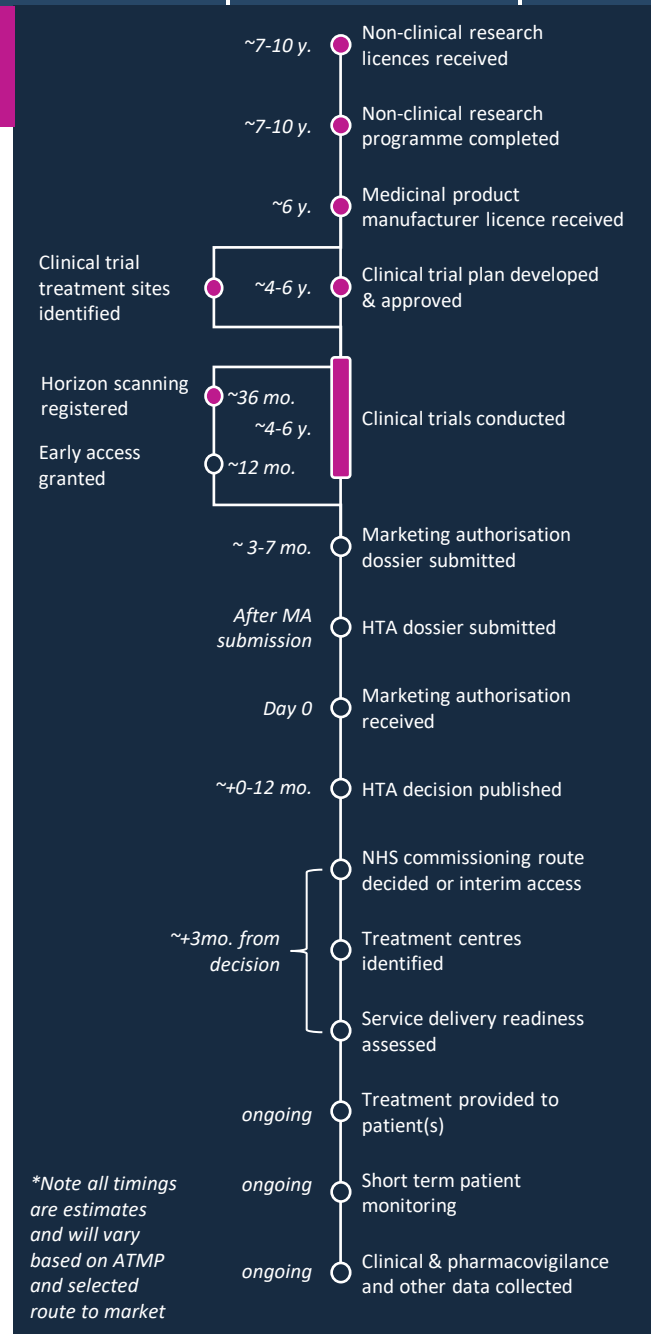
## To-do list

## Output

- ATMP developer

Permanent ILAP partners:
- MHRA
- NICE
- SMC
- AWTTC

**Linked steps** **Who is involved?** **Best practices & tips**



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

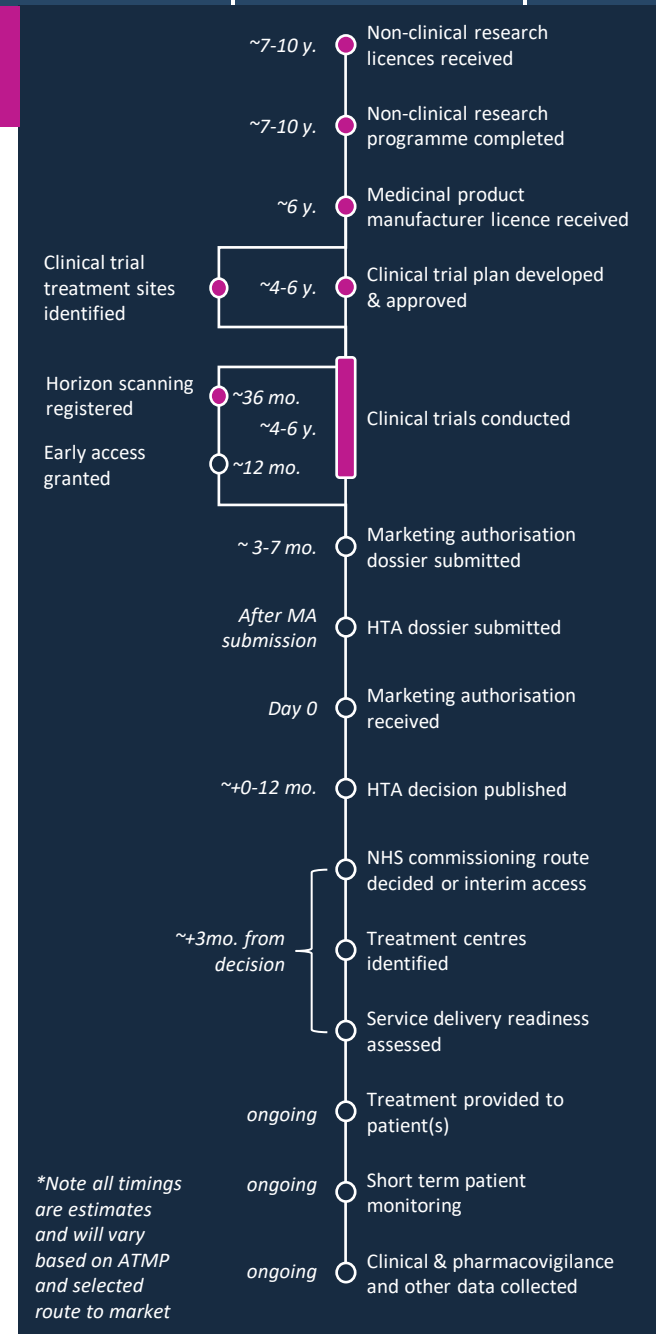
## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

Overview | To-do list | Output

- In order to maximise benefits of ILAP innovation passport, applications should be made early, during non-clinical research phase

**Linked steps** | **Who is involved?** | **Best practices & tips**



## KEY TOPICS

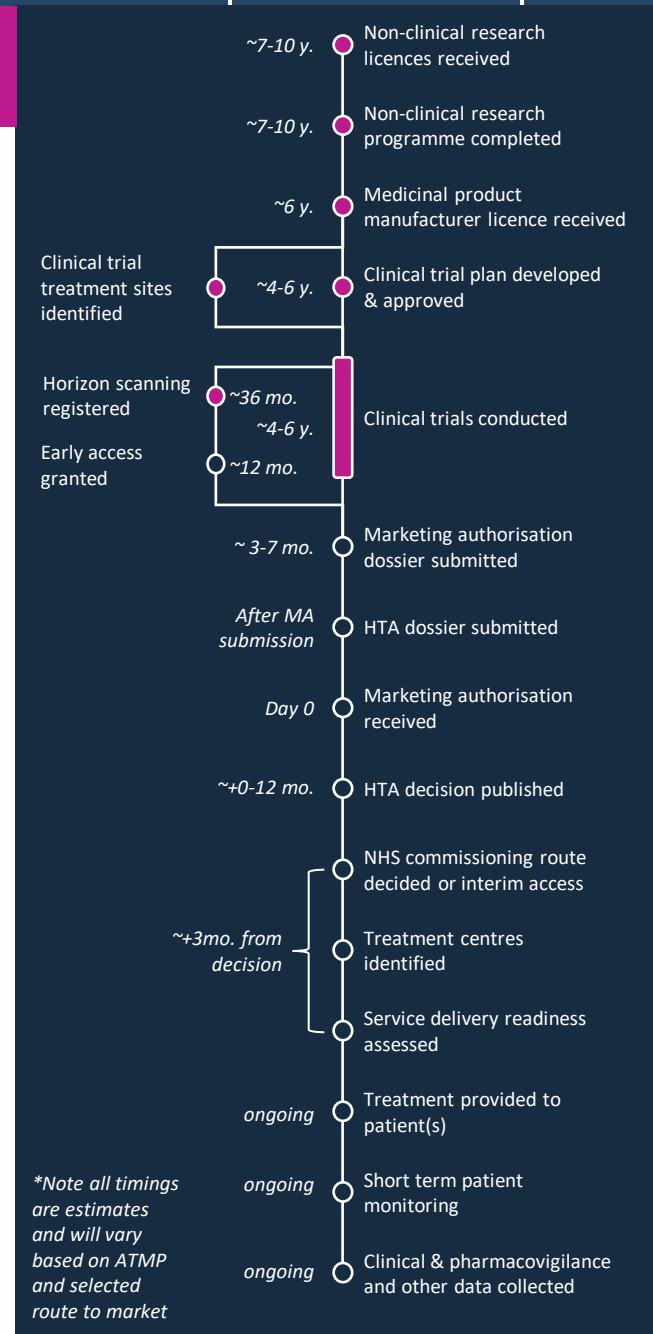


**Overview** | To-do list | Output

Developers of oncology products may submit a request to the MHRA to recommend their product for Project Orbis. Co-ordinated by the FDA, Project Orbis provides a route for concurrent review of marketing authorisation applications for promising cancer medicines from participating countries.

Applicants for Project Orbis are required to have an innovation passport designation, and will still be required to submit their full Marketing Authorisation to the MHRA using their existing process. There are fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

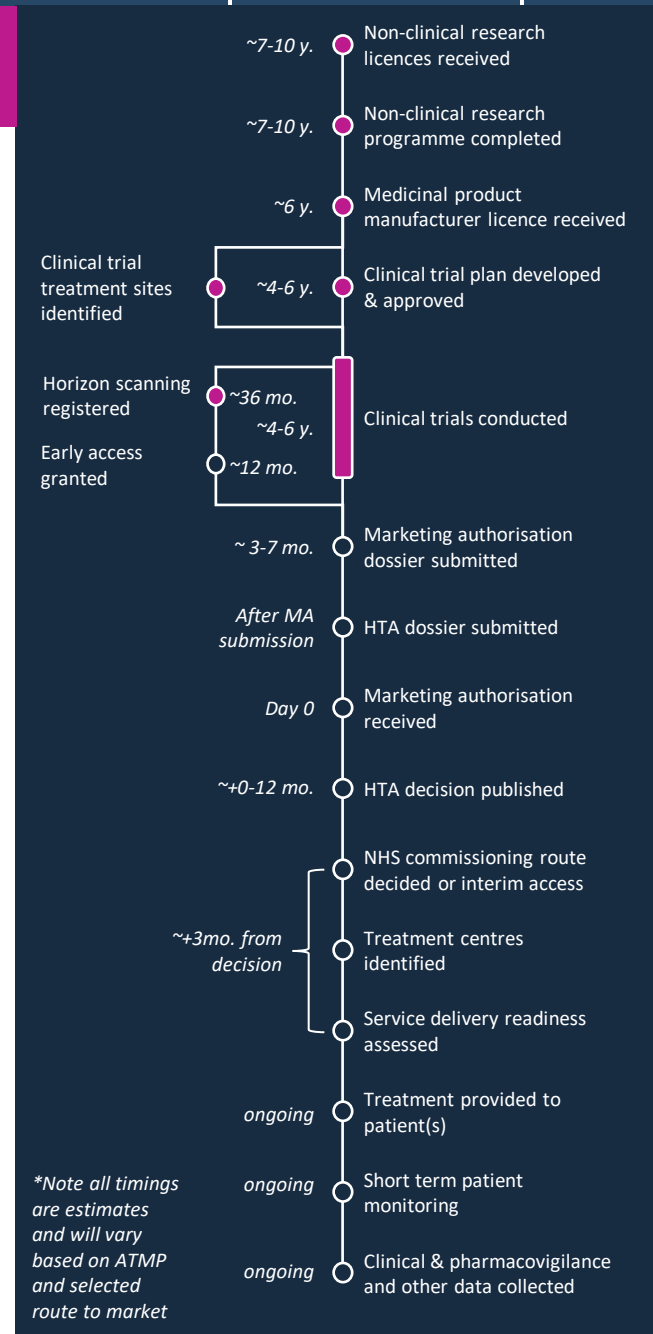
Overview | **To-do list** | Output

- Review Project Orbis guidance here and determine which submission type to use
- If not already completed, submit application through ILAP for Innovation Passport designation here
- Submit request (including a summary of the product and details of eligibility criteria) to the MHRA for them to recommend inclusion in Project Orbis to the FDA via Orbis-MHRA@mhra.gov.uk
- Submit meeting request to MHRA regarding Project Orbis submission via Orbis-MHRA@mhra.gov.uk
- Continue UK submission process along with concurrent submissions with participating countries
- Receive outcome decision from the FDA

### When

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

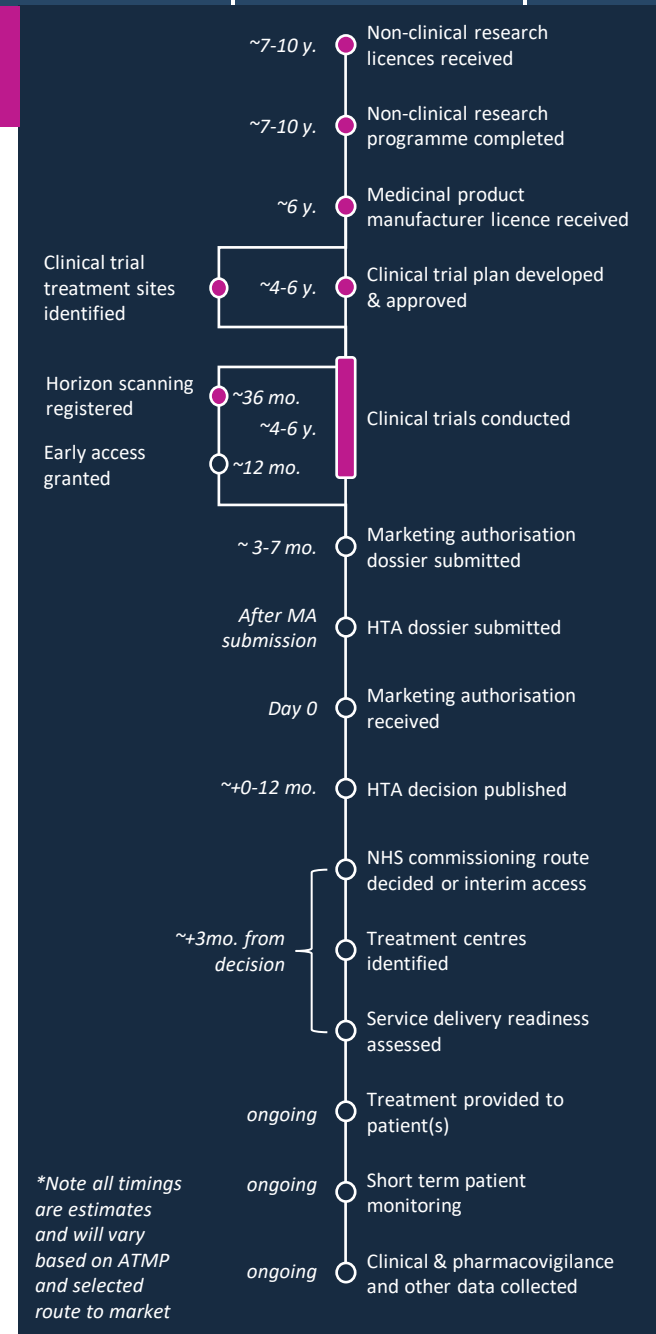
3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

Overview | To-do list | **Output**

- Inclusion or exclusion decision from FDA
- Marketing Authorisation decision from all participating Project Orbis countries



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

## To-do list

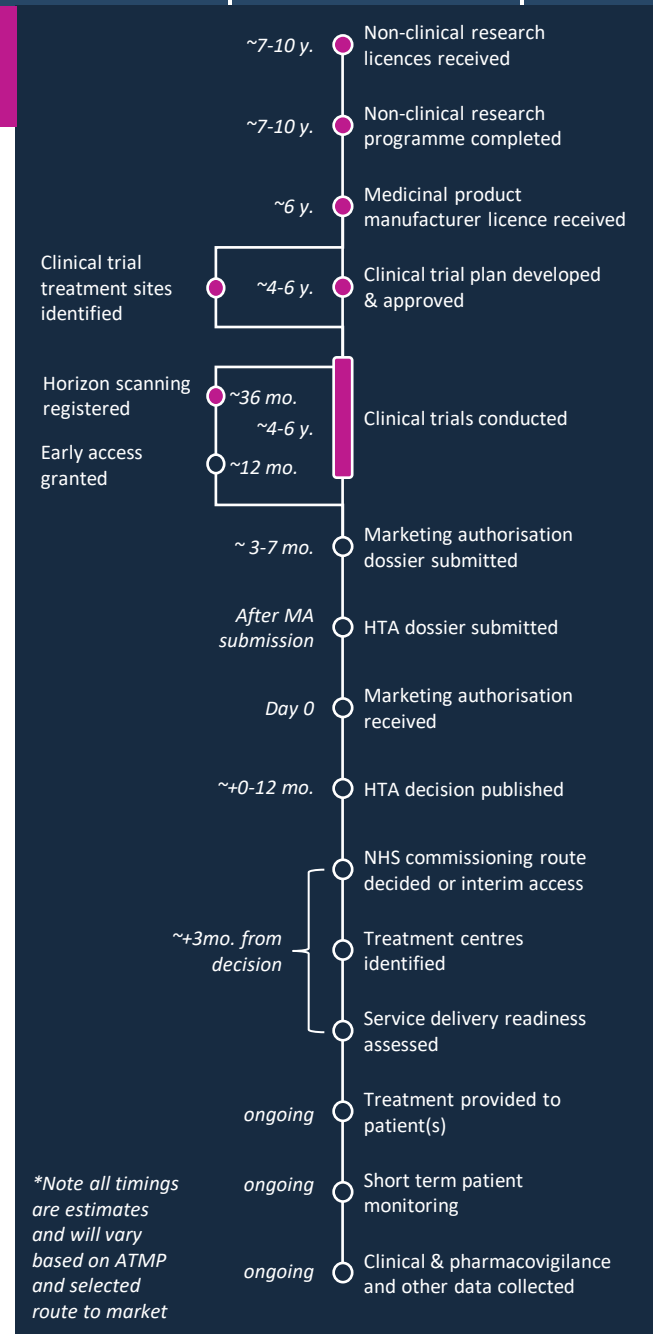
## Output

Marketing Authorisation submission

Innovative Licensing and Access Pathway (ILAP) [optional]

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

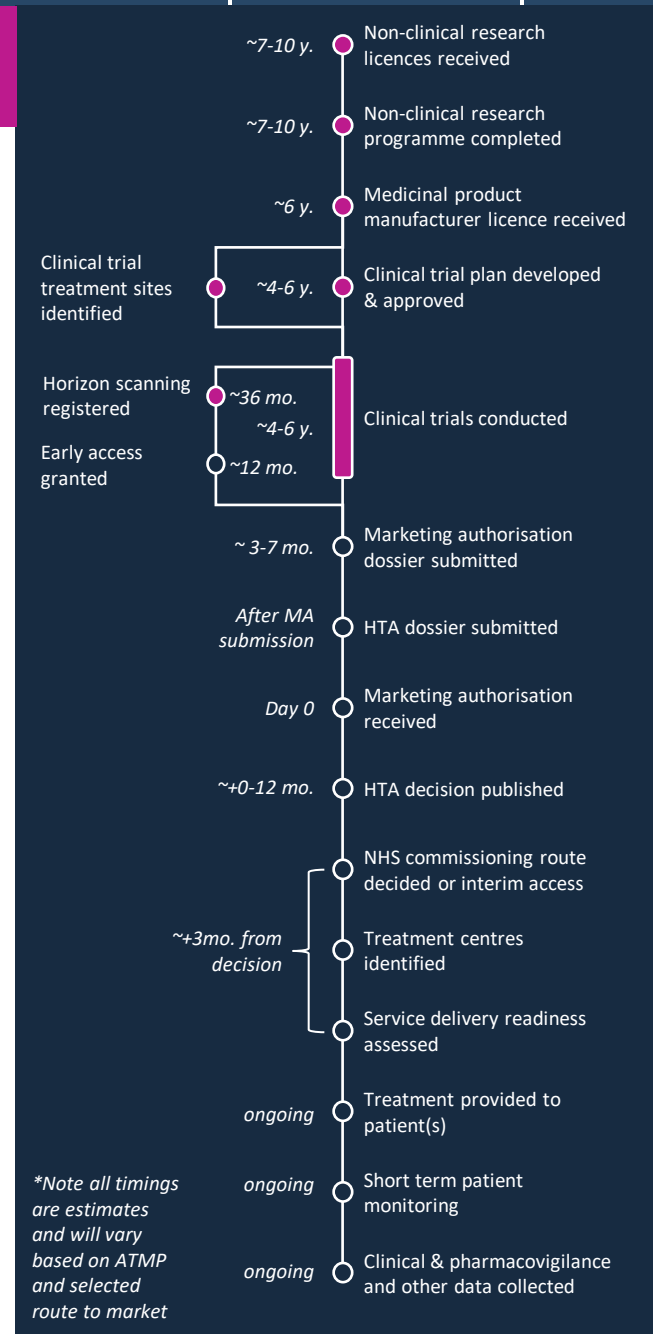
- ATMP developer
- MHRA
- FDA

Project Orbis participating countries:

- FDA (USA)
- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)
- ANVISA (Brazil)

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

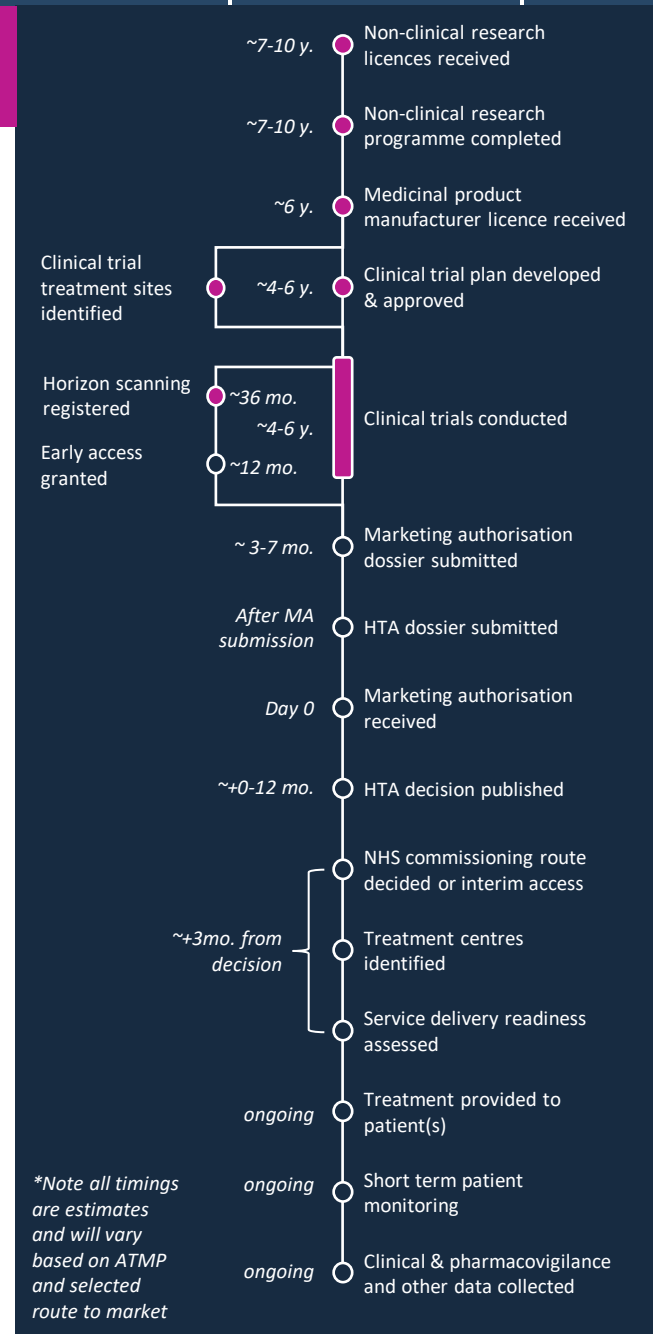
## Overview

## To-do list

## Output

- For queries relating to project Orbis, contact the MHRA at Orbis-MHRA@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

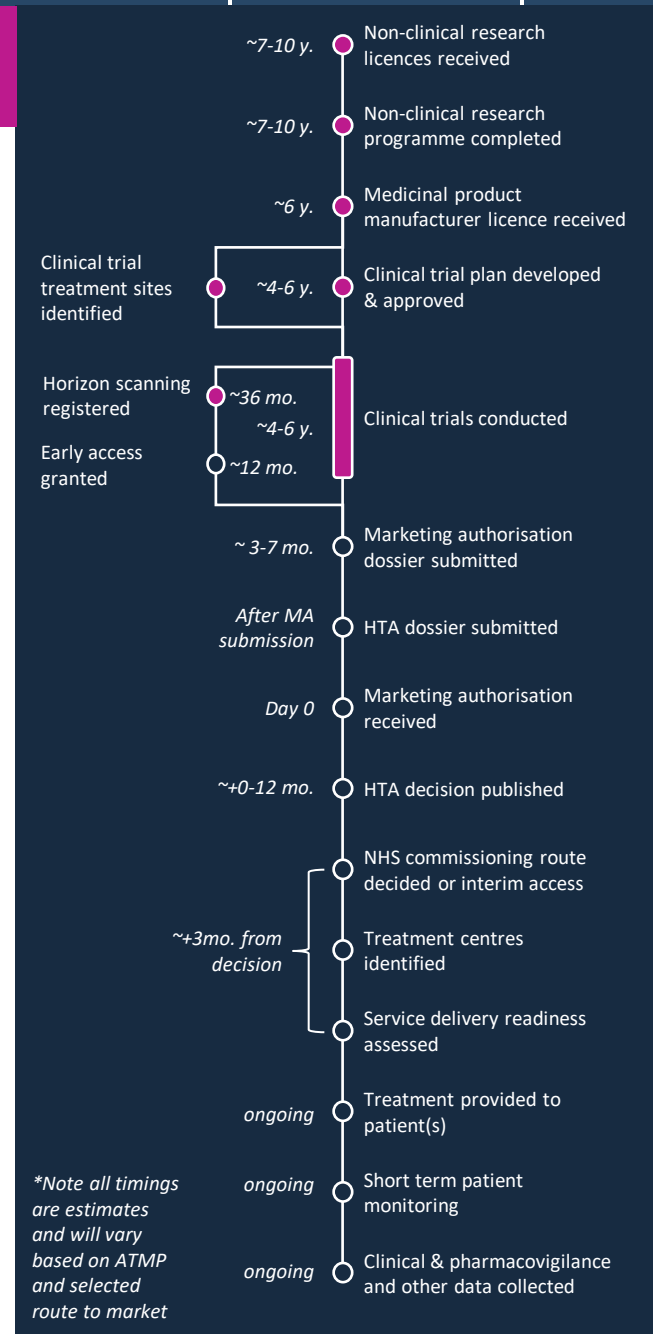


**Overview** | To-do list | Output

Developers can apply for a concurrent Marketing Authorisation submission and review in additional markets through the Access Consortium. There are a number of work sharing initiatives for different product types, so developers should review the guidance and ensure that it is relevant and applicable for their product.

Applicants for Access Consortium work sharing initiatives will still be required to submit their full Marketing Authorisation to the MHRA using their existing process, and will receive independent outcomes from participating countries. There are fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

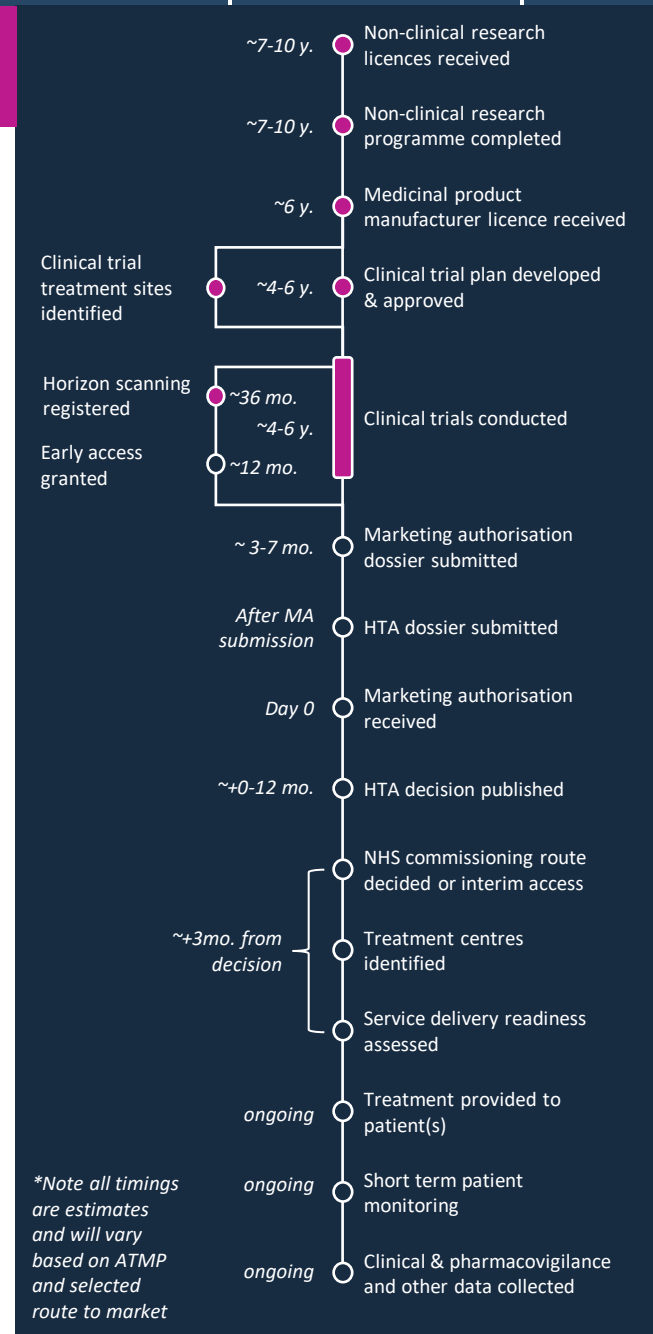
Overview | **To-do list** | Output

- Review Access Consortium guidance and determine if applicable for the product here
- Review the process for application in the New Active Substance (NAS) work sharing initiative here
- Express interest in the initiative using the expression of Interest (EOI) form available here, and submit to the MHRA (access-mhra@mhra.gov.uk) 3-6 months prior to MA submission
- Continue UK submission process along with concurrent submissions with participating countries (within 2 weeks of each other)

### When

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

3 **What programmes are available to accelerate time to market?**

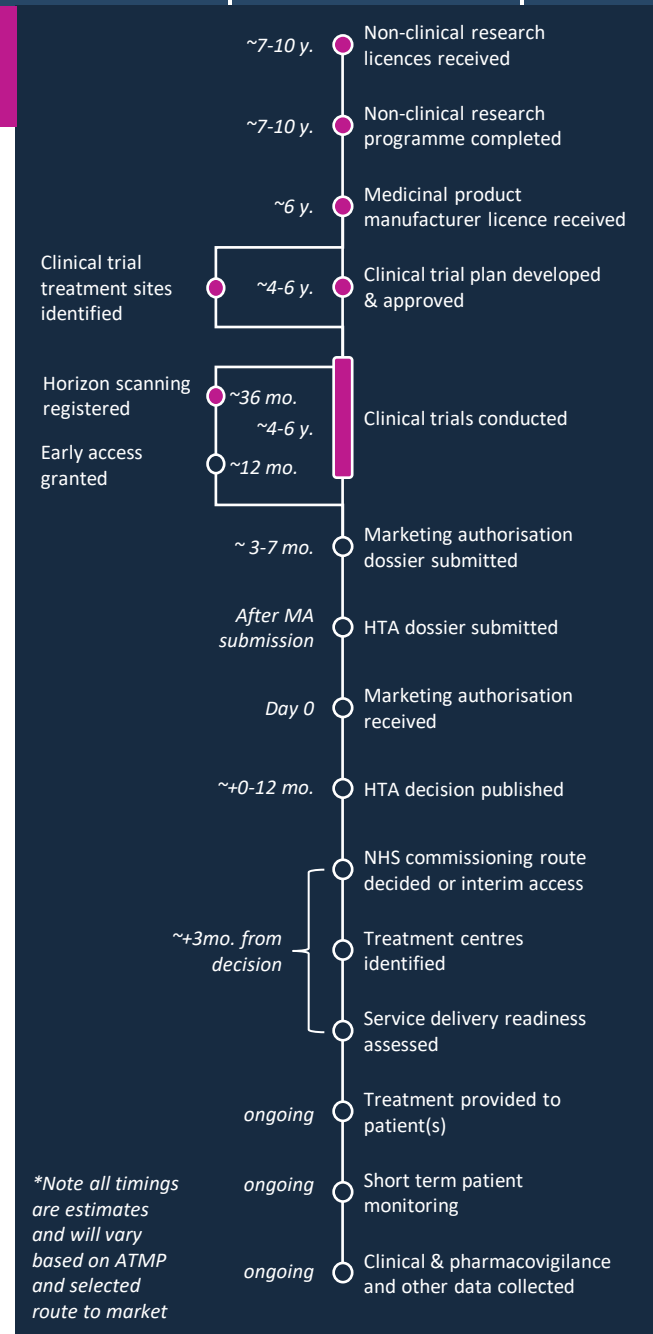
## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

Overview | To-do list | **Output**

- Co-ordinated review of Marketing Authorisation application
- Marketing Authorisation decision from all participating Access consortium countries

**Linked steps** **Who is involved?** **Best practices & tips**



1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

## Overview

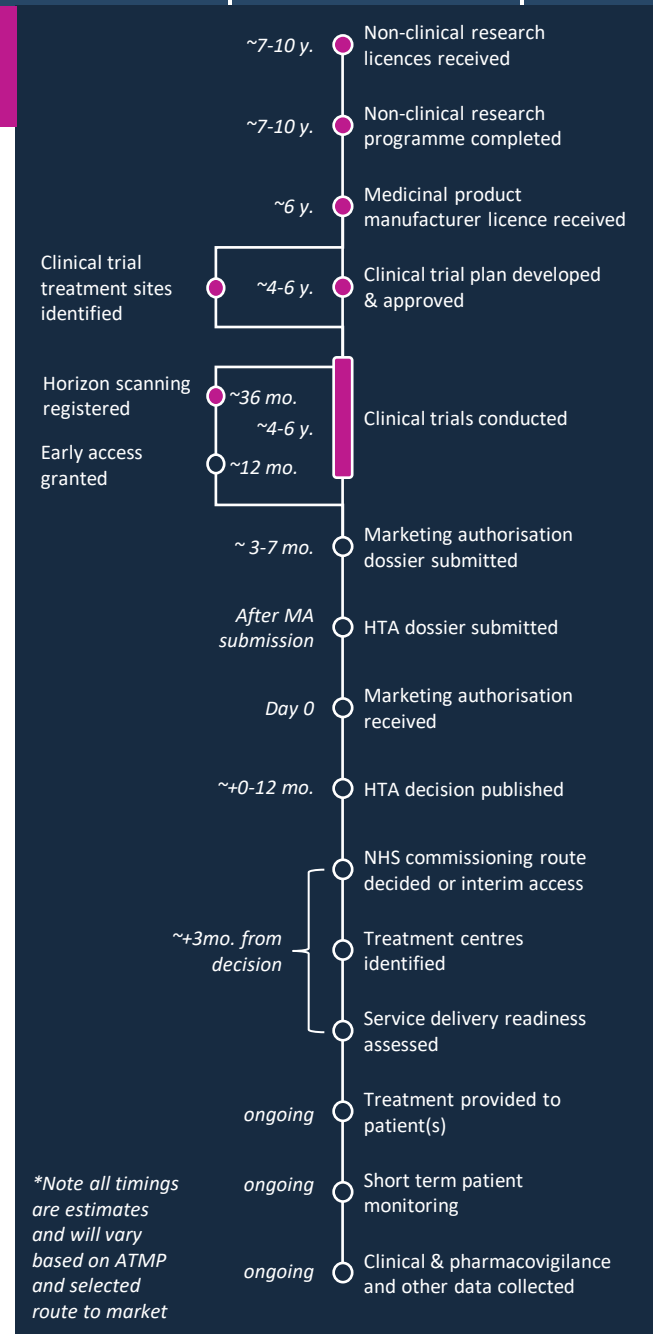
## To-do list

## Output

Marketing Authorisation submission

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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3 **What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

## Overview

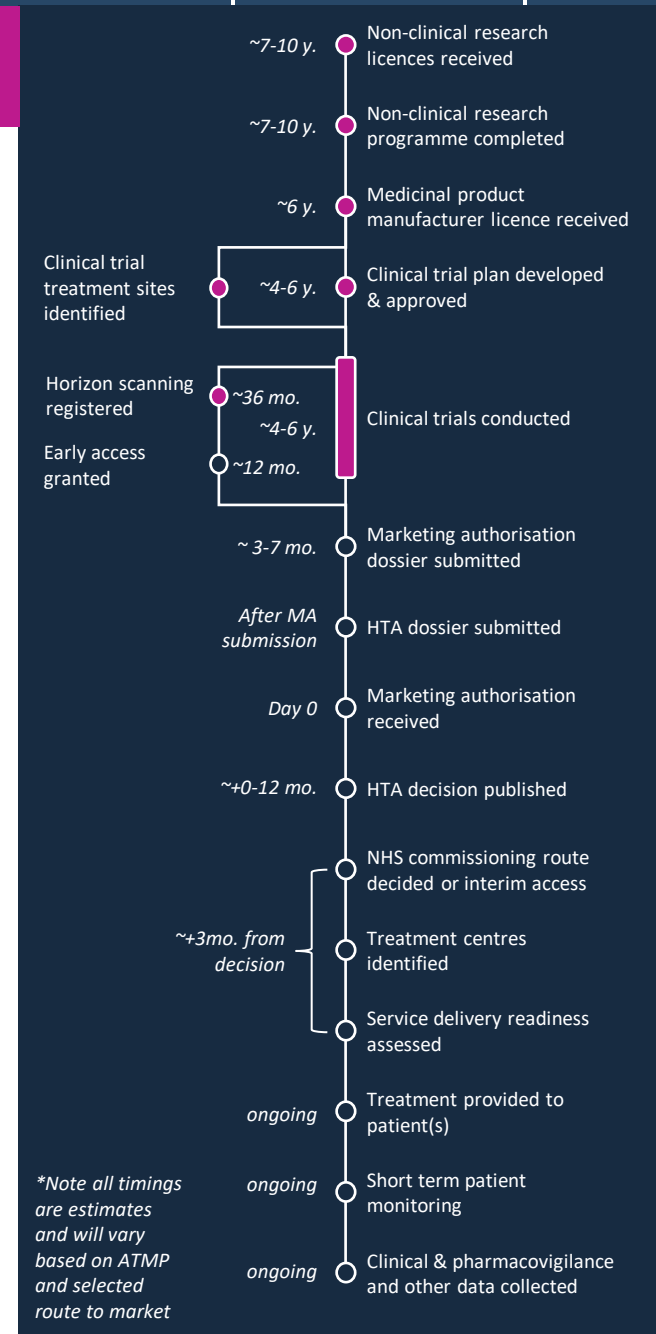
## To-do list

## Output

- ATMP developer
- MHRA

Access Consortium participating countries:

- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)




Linked steps | Who is involved? | Best practices & tips

1 What licences and/or approvals are required to conduct research?

2 What key regulatory steps are required to receive marketing authorisation?

**3 What programmes are available to accelerate time to market?**

## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

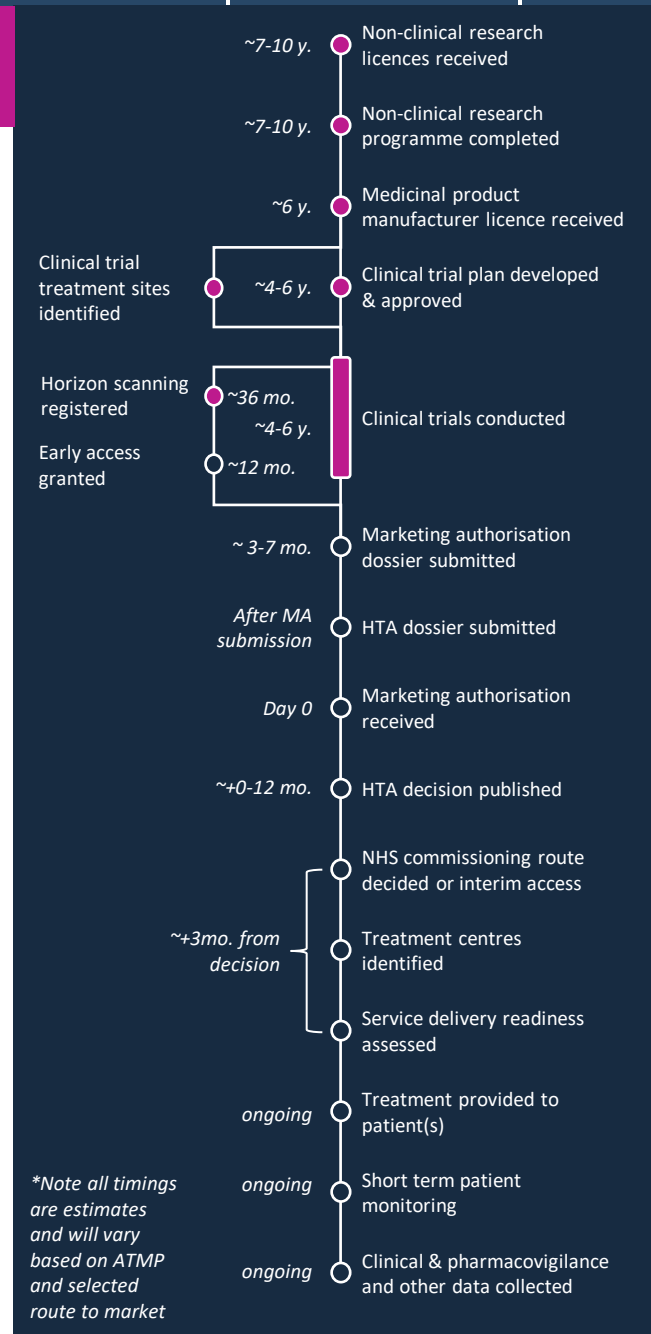
## Overview

## To-do list

## Output

- For queries relating to Access Consortium Work Sharing Initiatives, contact the MHRA at access-mhra@mhra.gov.uk

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **GxP compliance & certification**
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

**Overview** | To-do list | Output

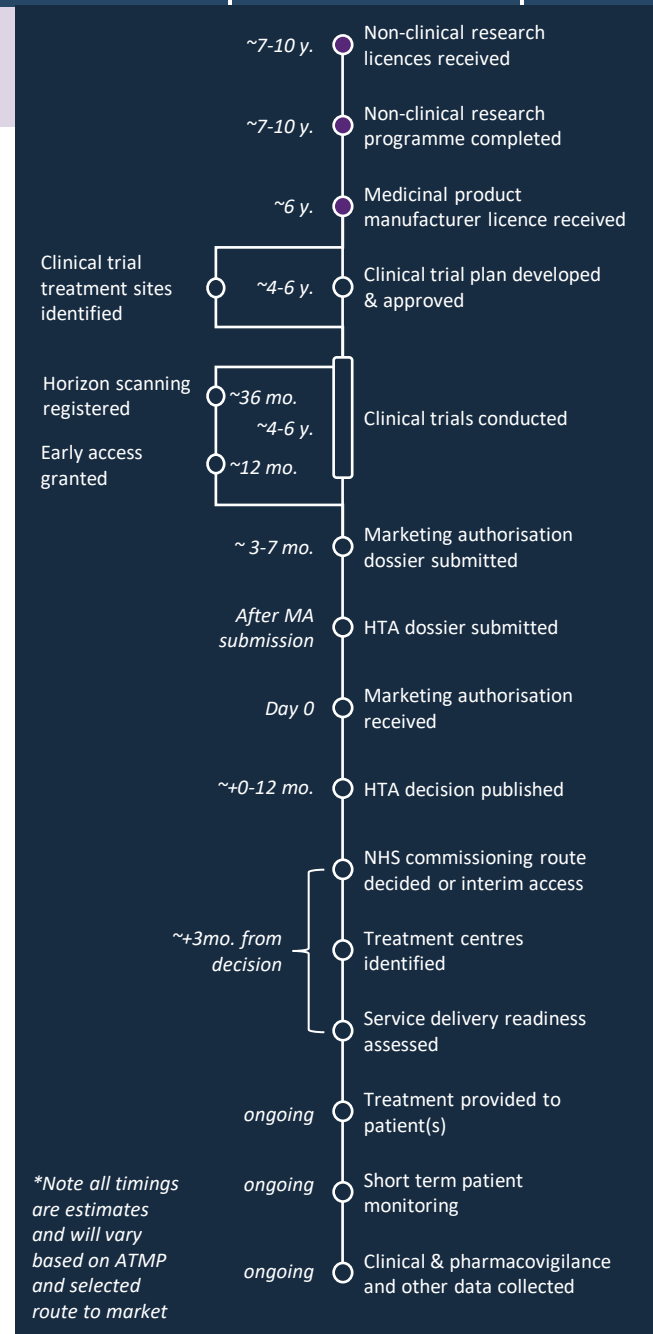
GxP should be central to the development of all ATMPs, including Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Pharmacovigilance Practice (GPvP) and if applicable, Good Distribution Practice (GDP).

Developers should review guidelines and resources from the EMA* on Good Manufacturing Practice (GMP) in relation to ATMPs to ensure compliance throughout the development and manufacturing phase, or if outsourcing, engage with identified GMP manufacturer.

The EMA has published GLP and GCP principles in relation to ATMPs to aid non-clinical study preparation. The MHRA also requires certification, inspection and membership of the UK GLP compliance monitoring programme run by the UK GLP Monitoring Authority (UK GLPMA). The programme is only open to facilities in the UK and requires a membership fee.

When planning clinical trials, compliance with Good Clinical Practice (GCP) requirements must be met and included in the trial design, this includes requirements for trial management, reporting and documentation.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

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- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

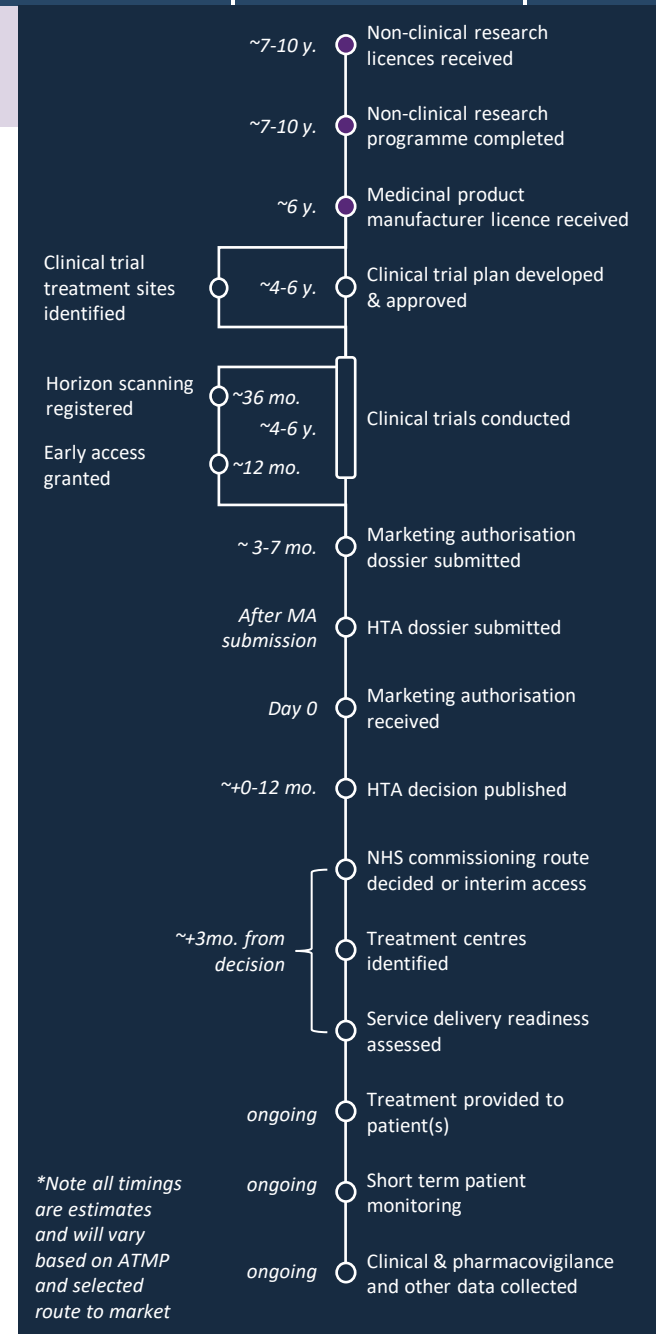
Overview | **To-do list** | Output

- Review guidelines and resources from the EMA on GMP in relation to ATMPs here
  - If outsourcing, engage with the identified manufacturer to ensure compliance with GMP
- Review GLP principles in relation to ATMPs here
- Review Q&A on use of materials of biological origin here
- Review UK-specific GLP guidance from the MHRA here
- Apply to the GLP compliance monitoring programme through the application form here
- Review EMA guidance on GCP guidelines and requirements for ATMPs here
- Review EMA ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) GCP guidelines here
- Review general guidance for preparing for conducting clinical trials in the UK here
- EMA guidance on Good Pharmacovigilance Practices (GPvP) can be found here with MHRA guidance on their application in the UK here
- Review MHRA guidance on Good Distribution Practice (GDP) here

**When**

GMP and GLP requirements should be met before commencing non-clinical research

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

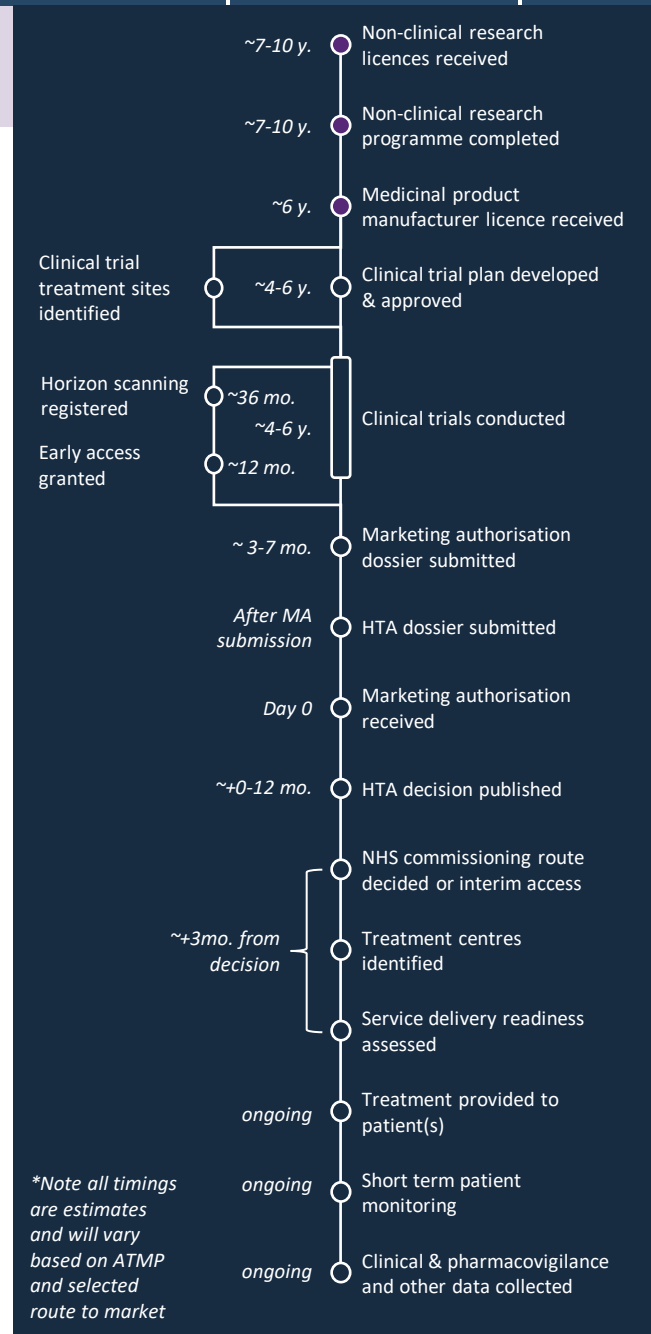
## KEY TOPICS

- **GxP compliance & certification**
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

Overview | To-do list | **Output**

- Guidance on GMP, GLP, GCP, GPvP and GDP for ATMPs reviewed and assessed
- GLP certification and membership of the UK GLP compliance monitoring programme

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **GxP compliance & certification**
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

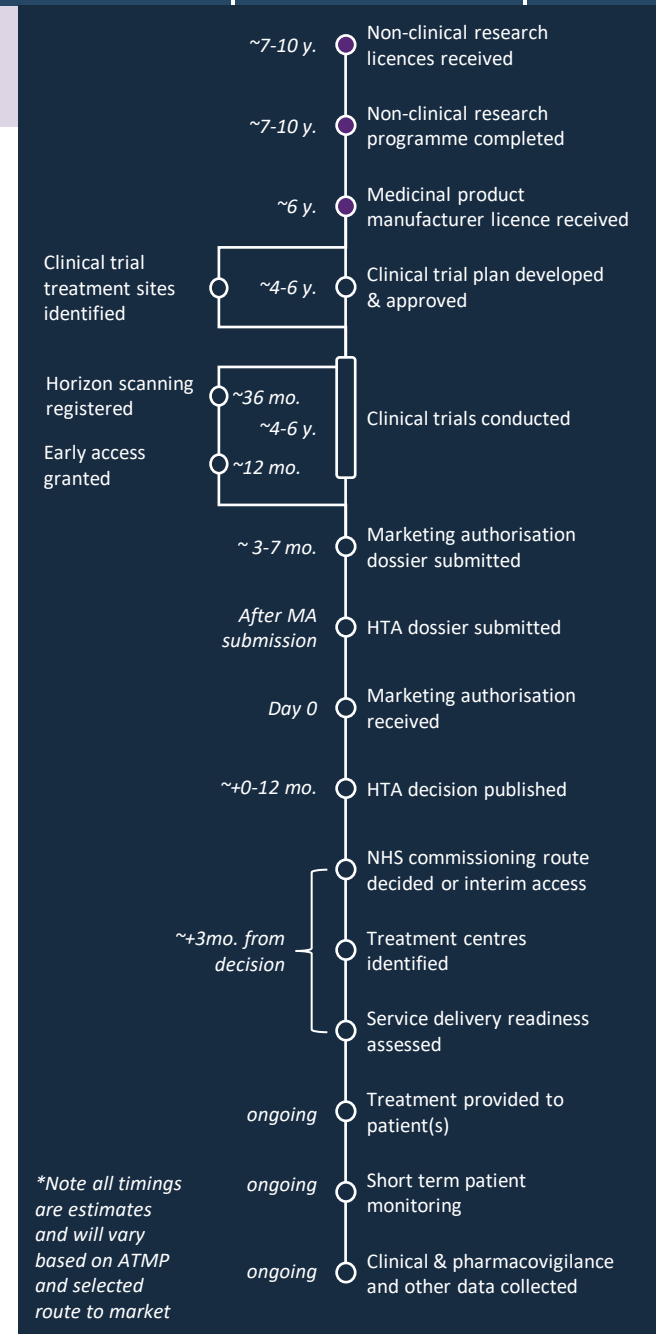
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **GxP compliance & certification**
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

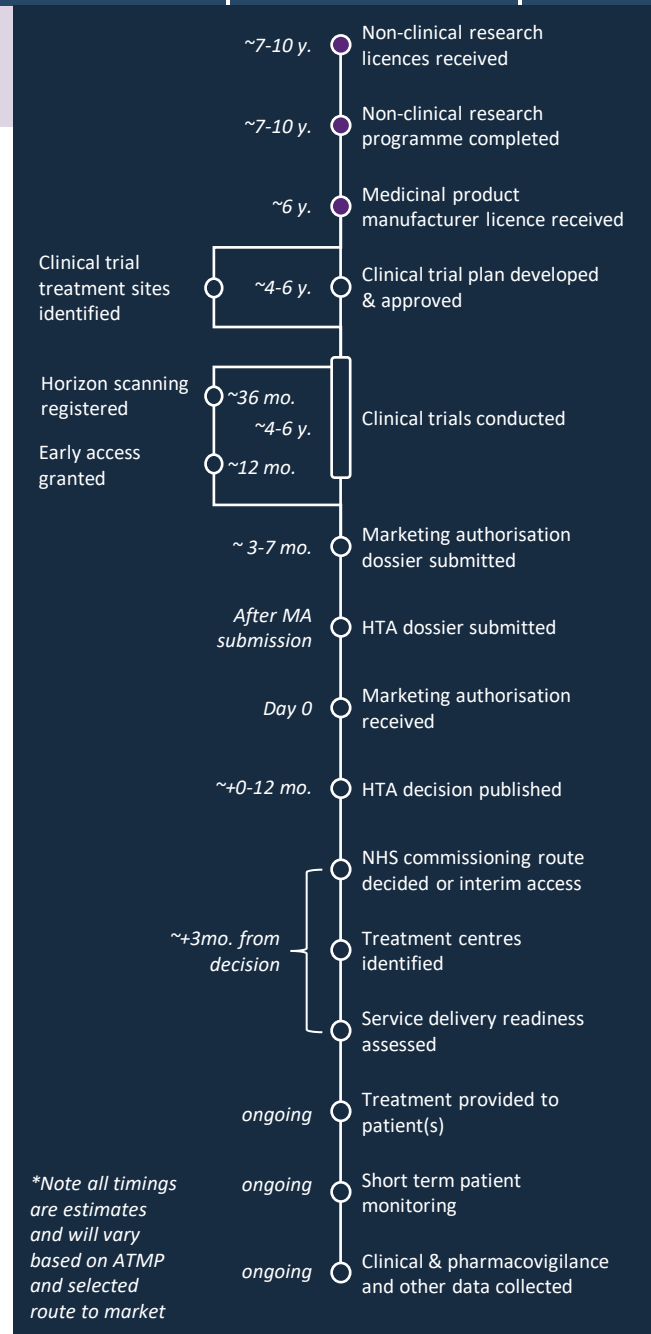
## Overview

## To-do list

## Output

- ATMP developer
- Manufacturing contractor (if applicable)
- Clinical trial sponsor
- MHRA
- UK GLP Monitoring Authority

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **GxP compliance & certification**
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

## Overview

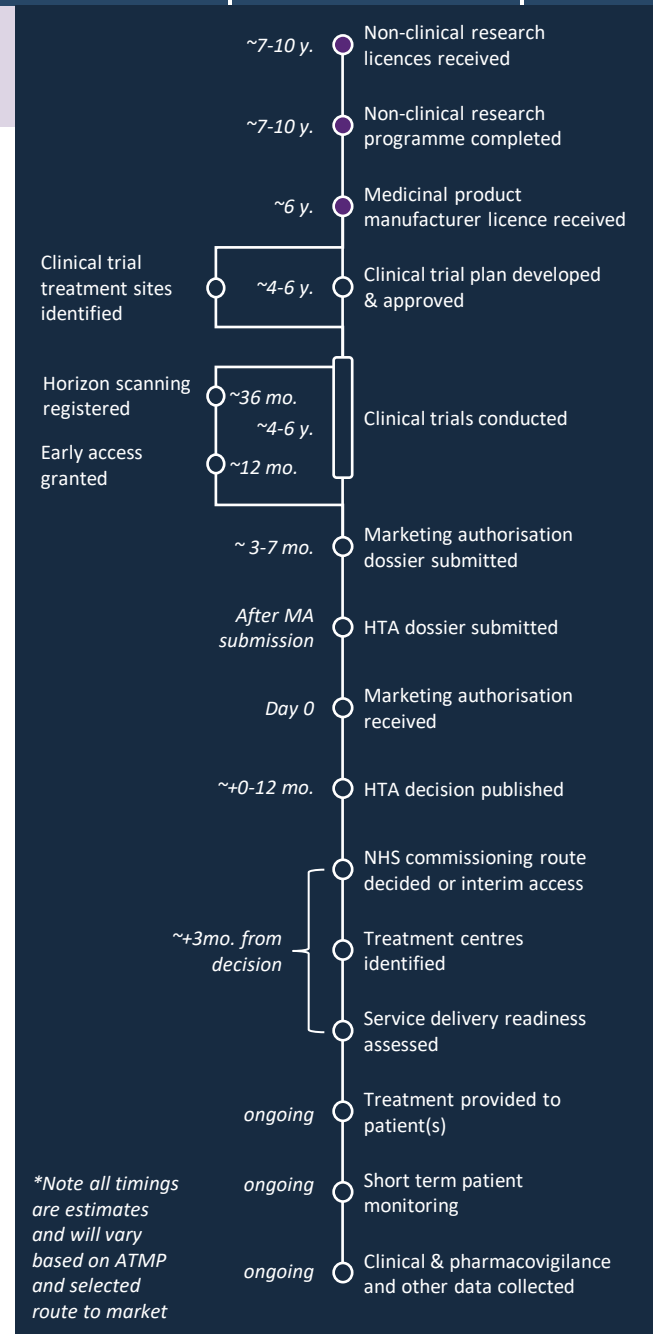
When manufacturing ATMPs for use in humans, key GMP requirements include but are not limited to an ATMP developer's:

- Quality system; premises and equipment; documentation; production and handling of ATMPs; cross contamination; control of starting and raw materials; handling human tissues and cells as starting materials; handling complaint & product recalls; out-of-specification handling; batch release process
- Developers can contact the GLPMA at gxplabs@mhra.gov.uk, and contact details for the various MHRA services can be found here

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



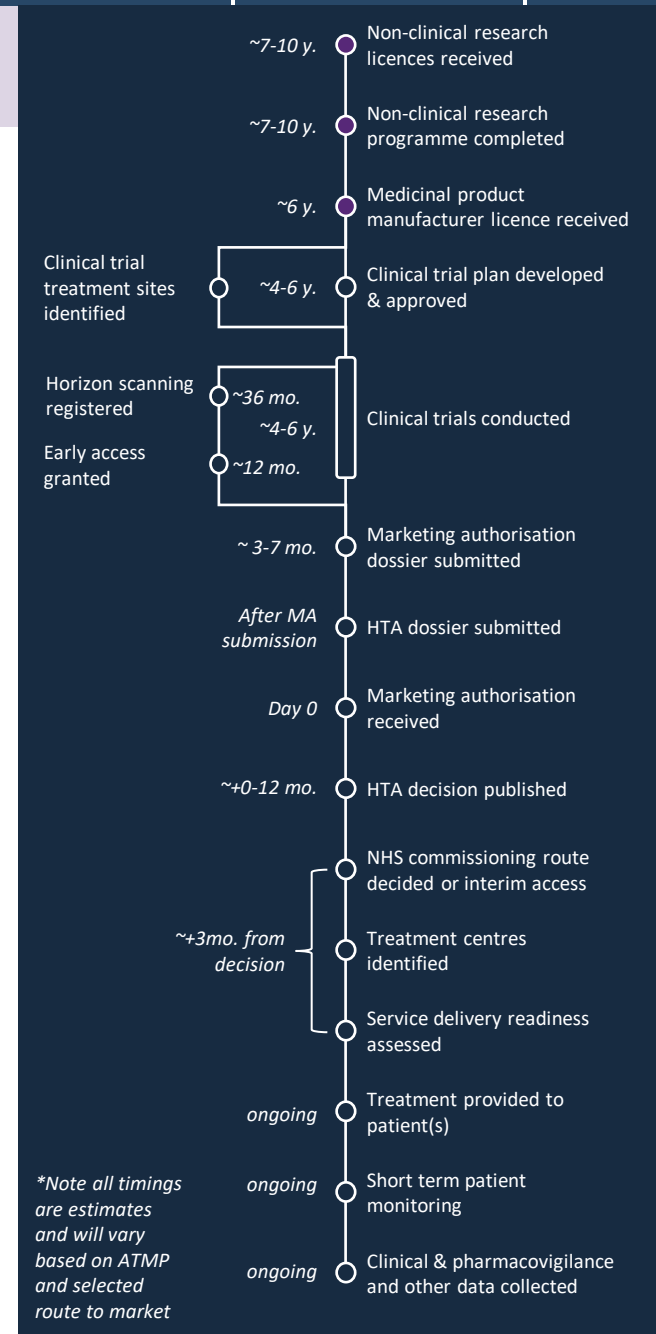
**Overview** | To-do list | Output

The Commission on Human Medicines (CHM) is a committee of the MHRA which has a number of expert advisory groups (EAG).

For perceived high risk trials (expected to apply to many ATMPs), the MHRA will seek advice from the Clinical Trials, Biologicals and Vaccines Expert Advisory Group (CTBVEAG) of the Commission on Human Medicines (CHM). First in Human (FIH) trials with novel compounds may be considered high-risk and likely to need assessment, so ATMP developers are recommended to reach out prior to clinical trial authorisation application to determine if an EAG assessment will be required.

Note: not all ATMP trials will require EAG assessment.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- GxP compliance & certification
- **Expert Advisory Group Clinical Trial Assessment [if applicable]**
- Clinical trial planning, design & protocol development
- Governance & process documentation
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- Trial recruitment

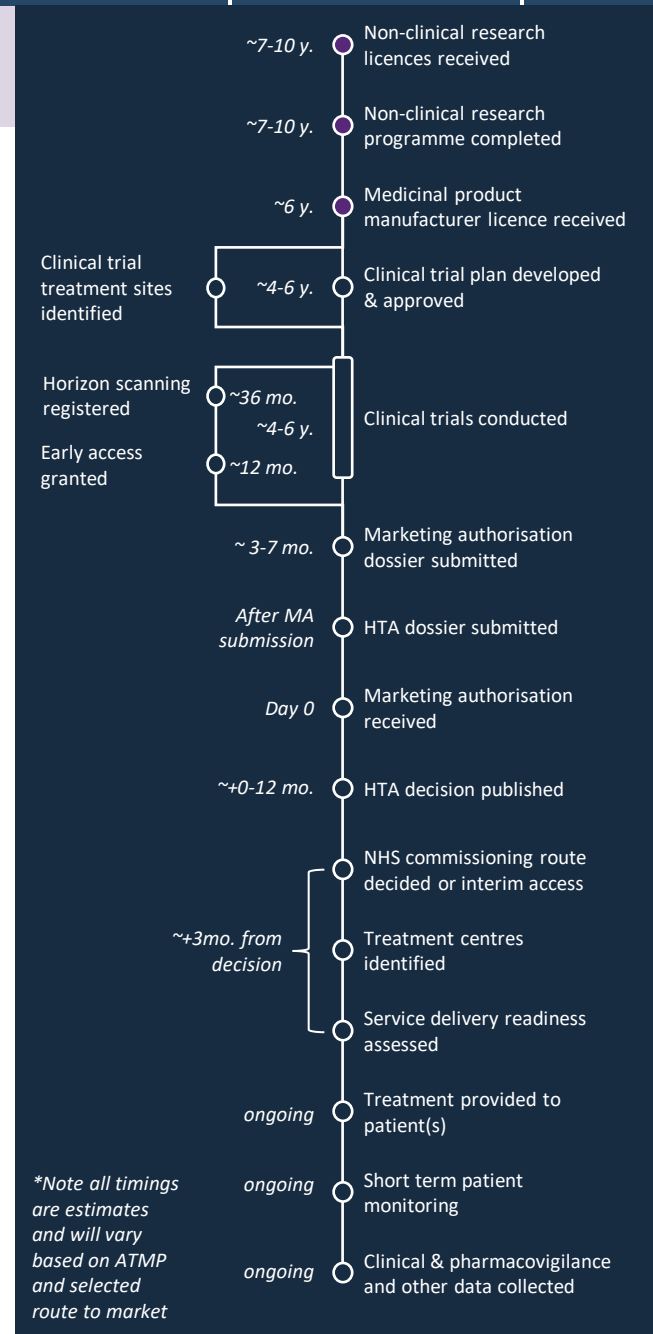
Overview | **To-do list** | Output

- To get advice on whether EAG assessment is required pre-submission, developers should review the guidance here and email clintrialhelpline@mhra.gov.uk
- If EAG assessment is required, developers/sponsors should then select the date for the EAG meeting
- Developers should then prepare the submission package and send it to clintrialhelpline@mhra.gov.uk 21 days prior to the EAG meeting

### When

- Prior to Clinical Trial Application (CTA) submission
- The MHRA will respond within 14 days

**Linked steps** | **Who is involved?** | **Best practices & tips**



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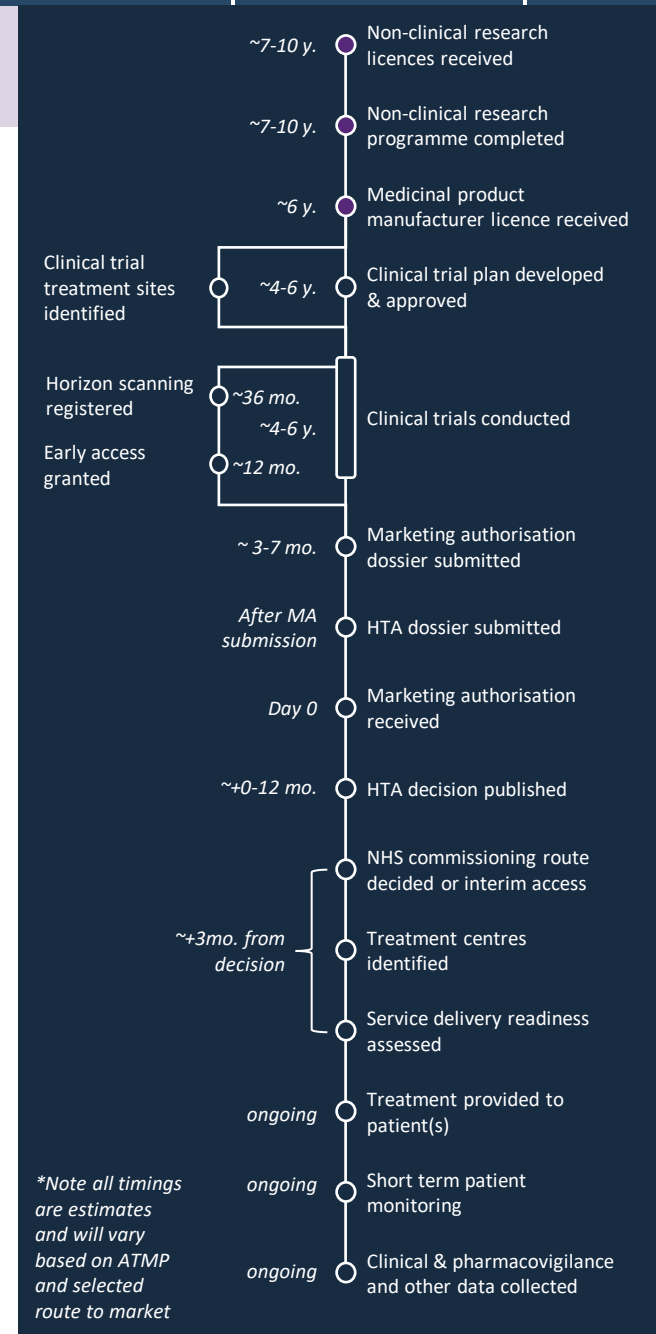
Overview | To-do list | **Output**

- Decision on whether EAG assessment is required
- EAG assessment component of clinical trial approval process

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

## To-do list

## Output

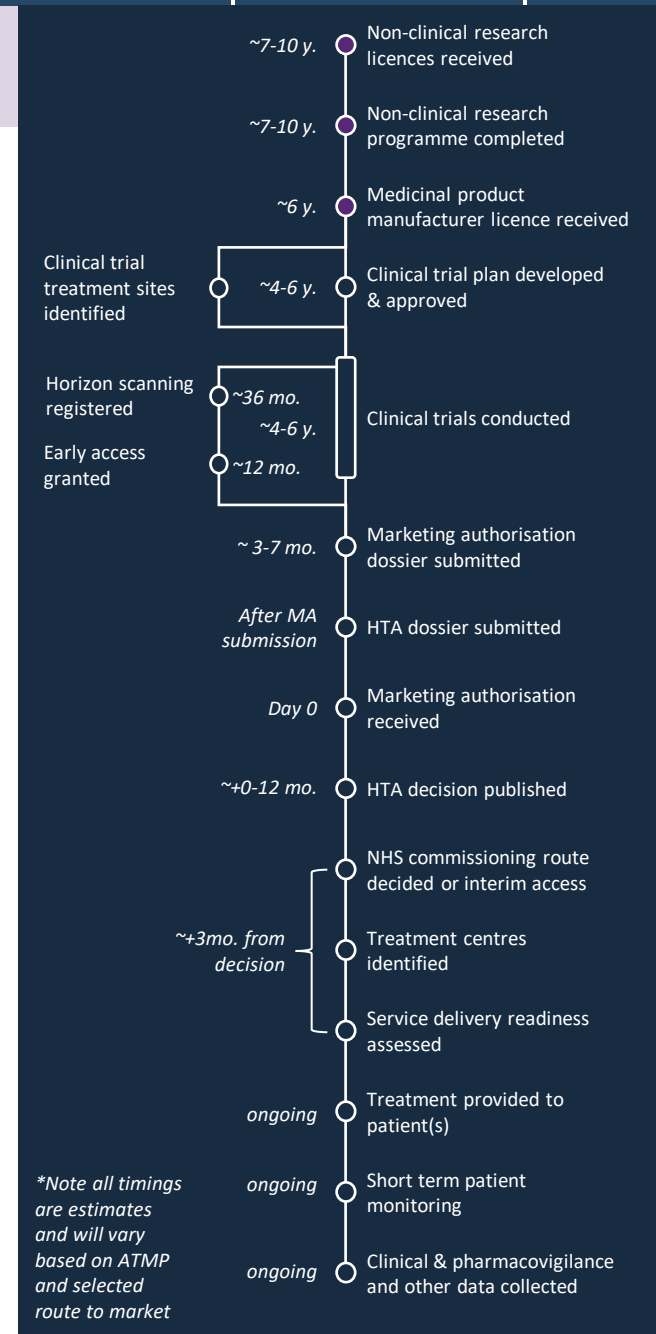
Regulatory and/or scientific advice

Clinical trial planning, design & protocol development

**Linked steps**

**Who is involved?**

**Best practices & tips**



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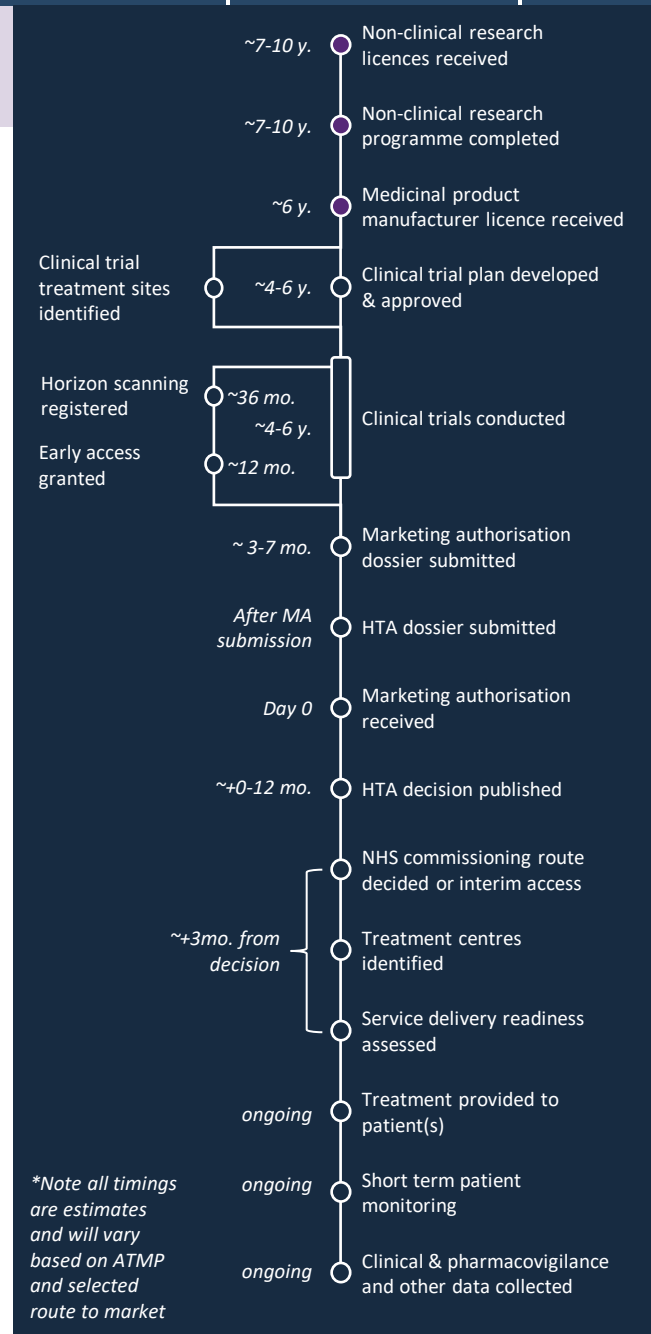
## Overview

## To-do list

## Output

- ATMP developer
- CHM of the MHRA

**Linked steps** **Who is involved?** **Best practices & tips**



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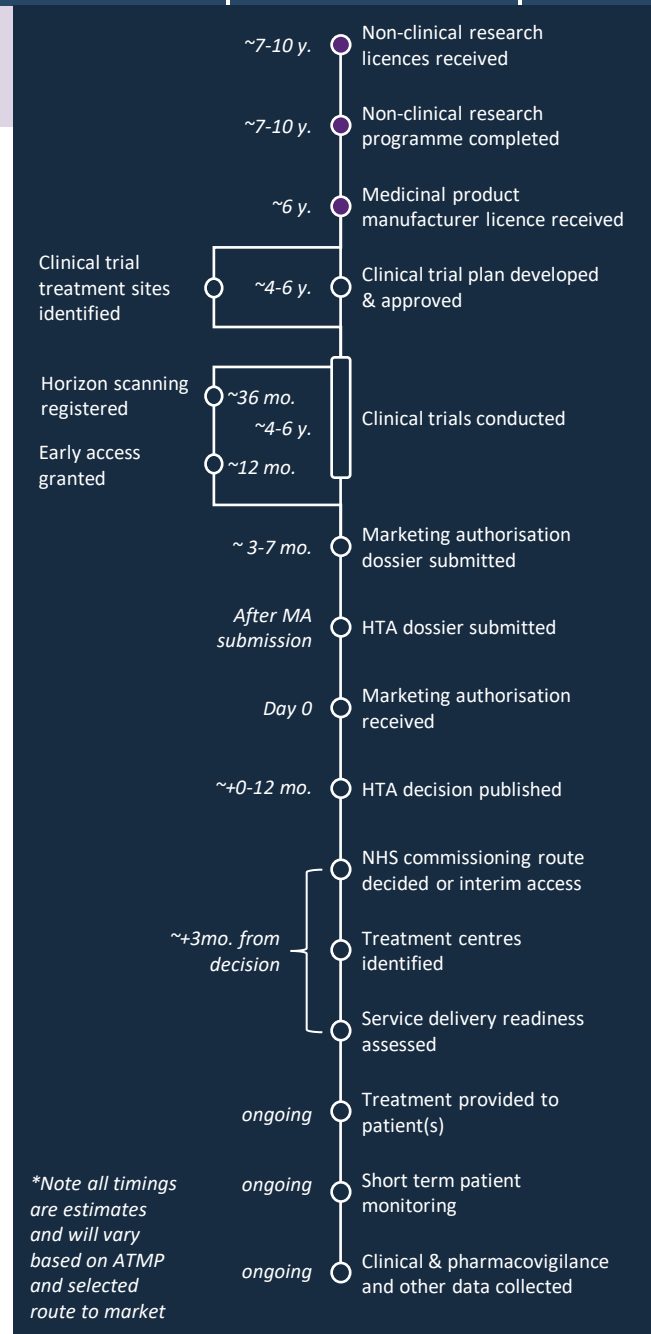
## Overview

- If EAG assessment is required, developers and trial sponsors must be prepared for ongoing engagement during the assessment once CTA has been submitted

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



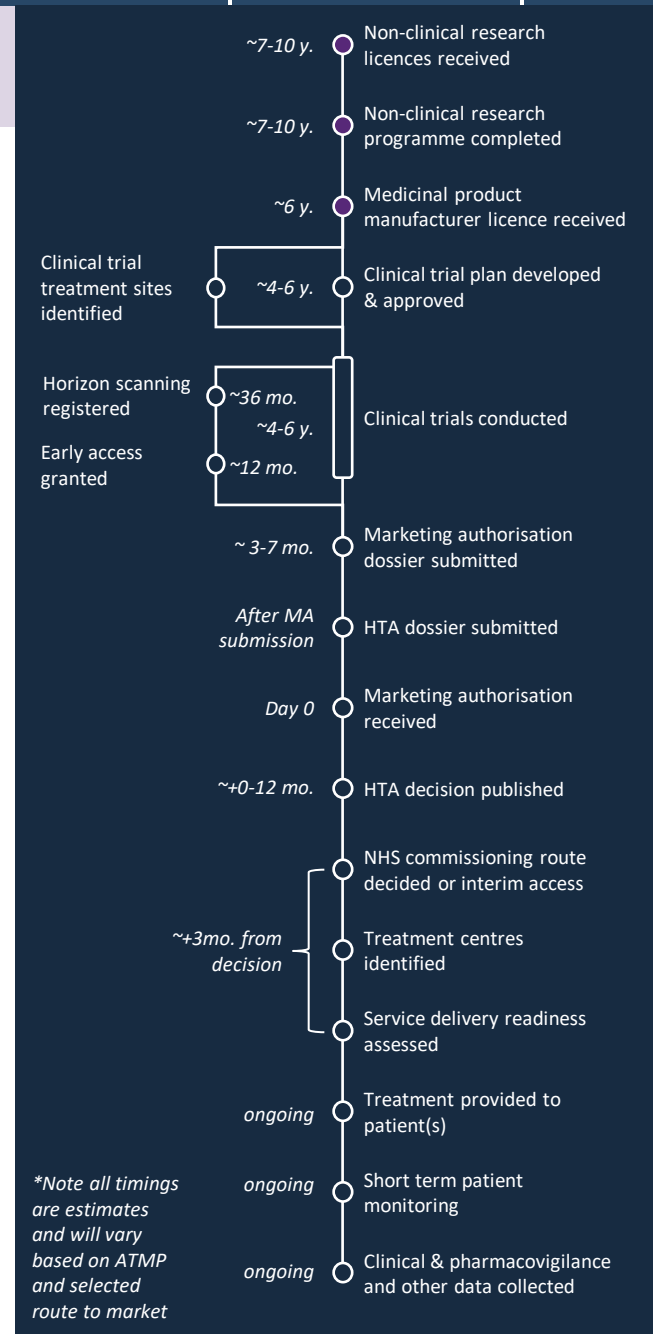
**Overview** | To-do list | Output

Developers should review the resources and guidance available to ensure that all of the relevant factors are considered and incorporated into ATMP clinical trial design. The clinical trial design and plan should be well documented as they will be required for regulatory approvals and permissions.

Once a trial plan and design has been completed, ATMP developers must develop and confirm their clinical trial Protocol.

ATMP developers should ensure that all operational clinical trial stakeholders have been identified and confirm that they are aware of their roles and responsibilities, escalation procedures and reporting requirements.

**Linked steps** **Who is involved?** **Best practices & tips**



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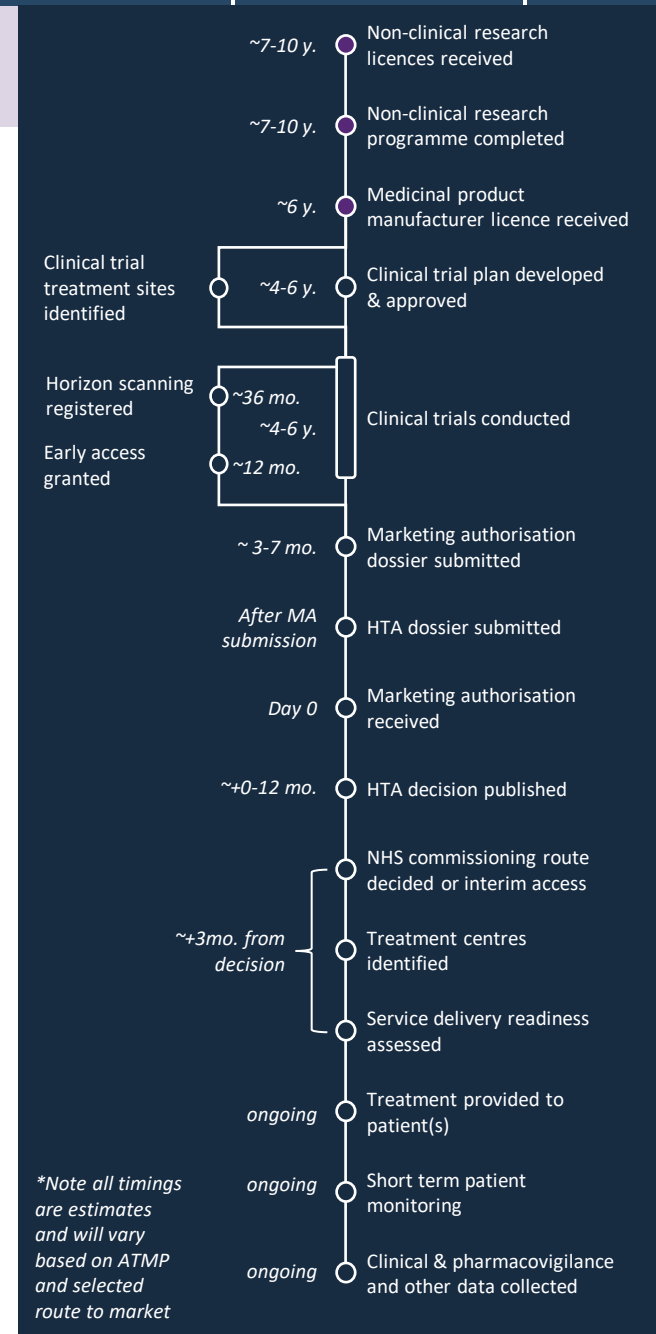
Overview | **To-do list** | Output

- Review the full clinical trial toolkit developed by the NIHR here
  - Guidance on trial planning and design can be found here
    - Guidance from the MHRA on common issues identified during clinical trial applications here
    - To request MHRA advice on clinical trial design contact the Clinical Trials Helpline: clintrialhelpline@mhra.gov.uk
  - Guidance on risk assessments can be found here
    - EMA guidelines on conducting environmental risk assessments for human use can be found here
  - Guidance on investigator selection and site feasibility can be found here
  - Guidance on trial management and monitoring can be found here
  - NIHR resources on patient & public involvement (PPI) can be found here
  - Confirm trial funding (if applicable)
- Review ATTC network on clinical trial design for ATMPs here
- Review guidance on trial Protocol development here
- Review HRA trial Protocol templates here

**Next >**

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



Overview | **To-do list** | Output

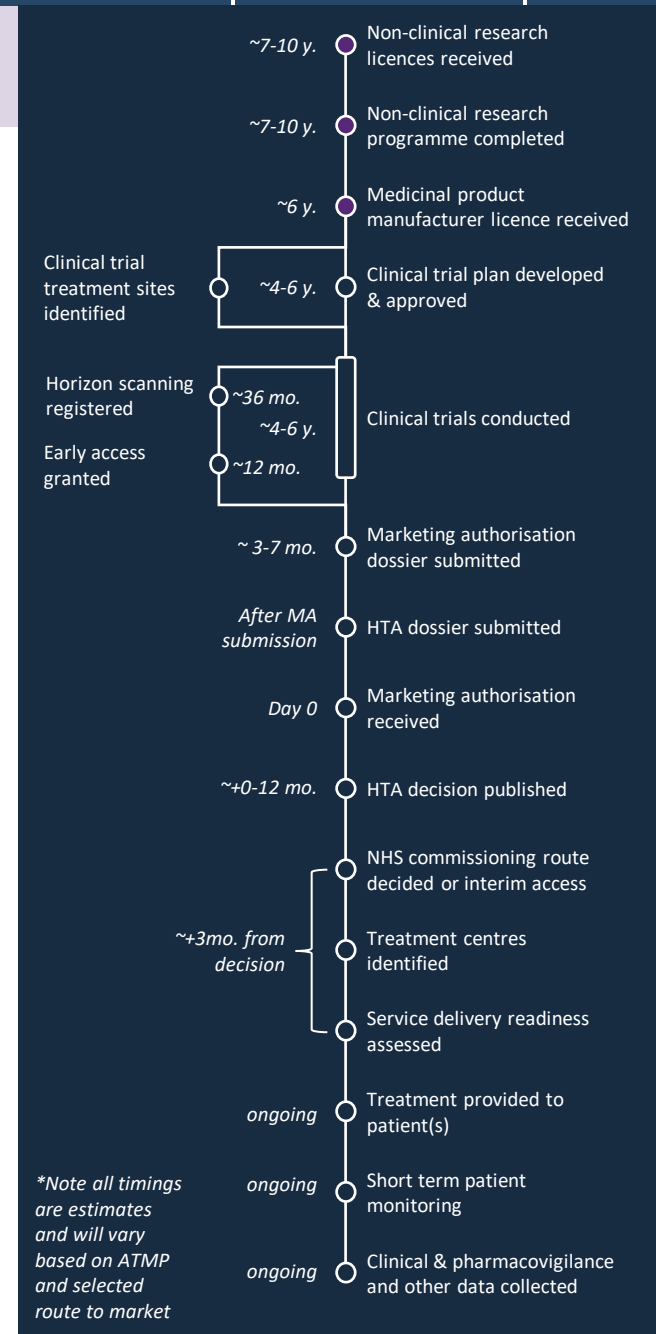
- Identify and confirm clinical trial stakeholders (including trial sponsor) and ensure awareness of roles and responsibilities
- For combination ATMPs including a medical device component, a concurrent clinical investigation may be required, see guidance here
- Developers are recommended to review guidance from the NHS Specialist Pharmacy Service here, highlighting implementation challenges faced by the NHS and design considerations to minimise them

### When

Prior to Clinical Trial Application

**< Previous**

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

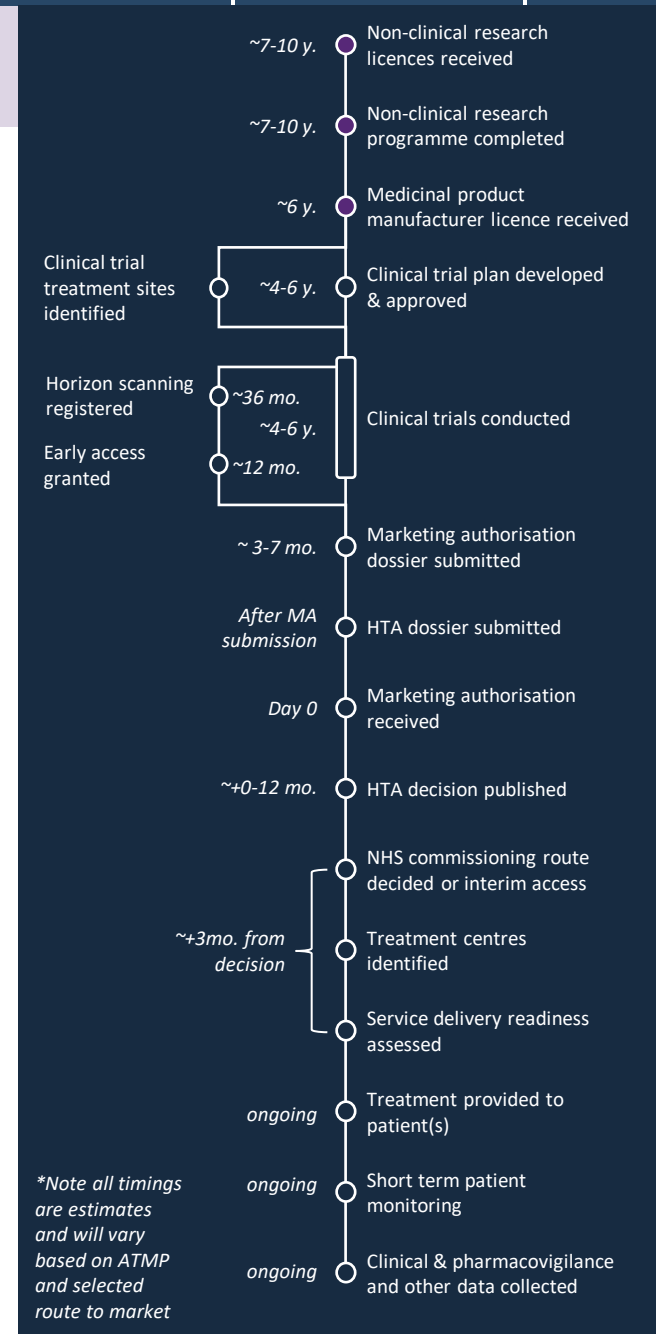
## KEY TOPICS



Overview | To-do list | **Output**

- Documented clinical trial design and detailed plan
- Investigators and Sponsor
- Trial sites confirmed
- Trial Protocol

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- GxP compliance & certification
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- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

## Overview

Regulatory and/or scientific advice

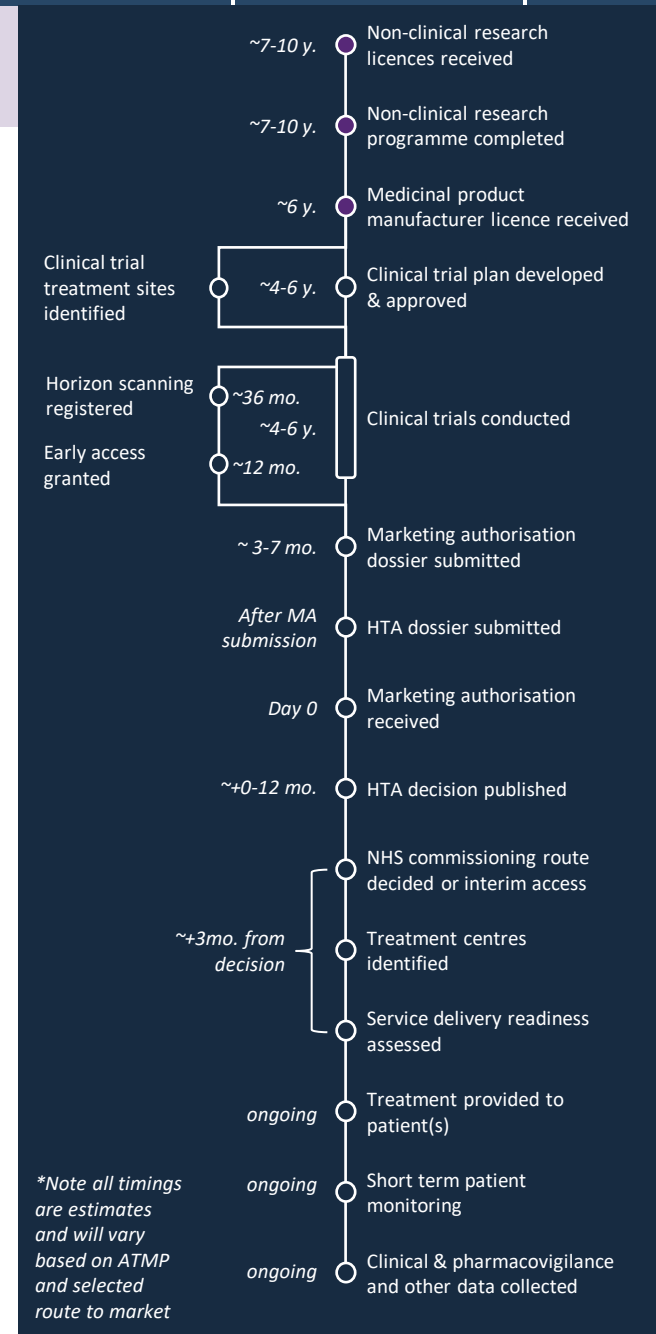
GxP compliance & certification

Service delivery readiness

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

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## KEY TOPICS

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- Trial recruitment

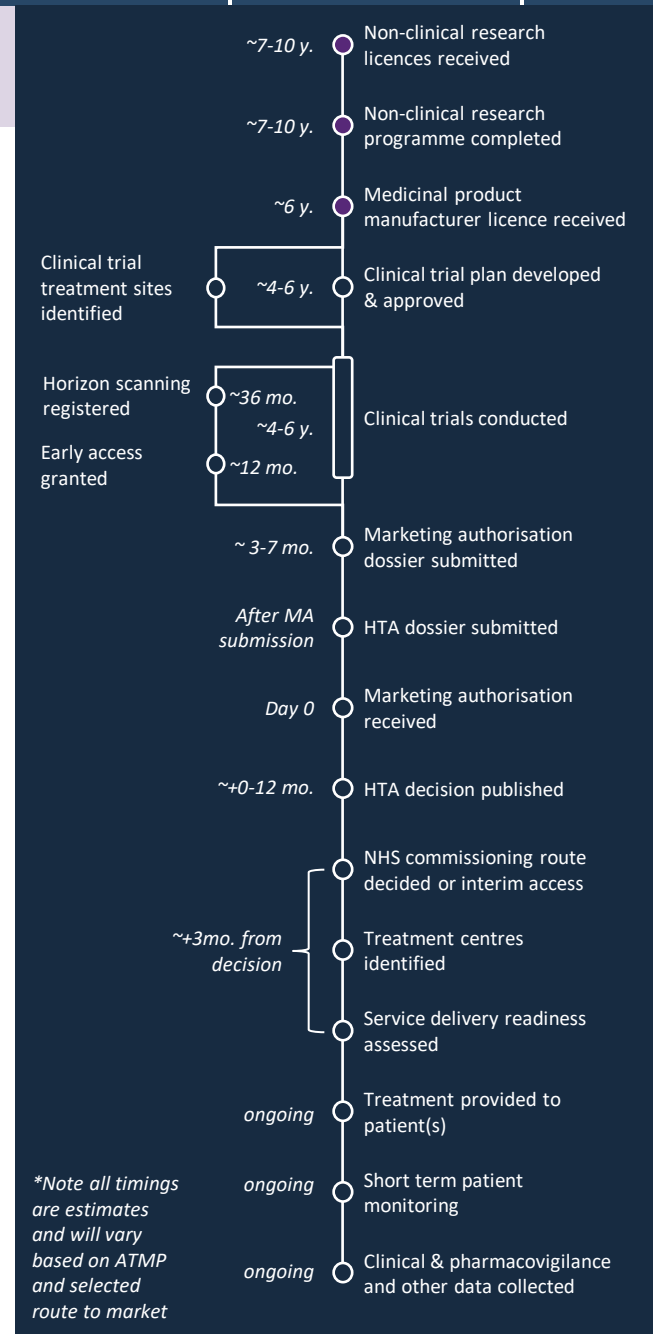
## Overview

- ATMP developer
- Patient groups
- Trial sponsor
- Principal Investigator(s)
- Trial sites
- MHRA

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

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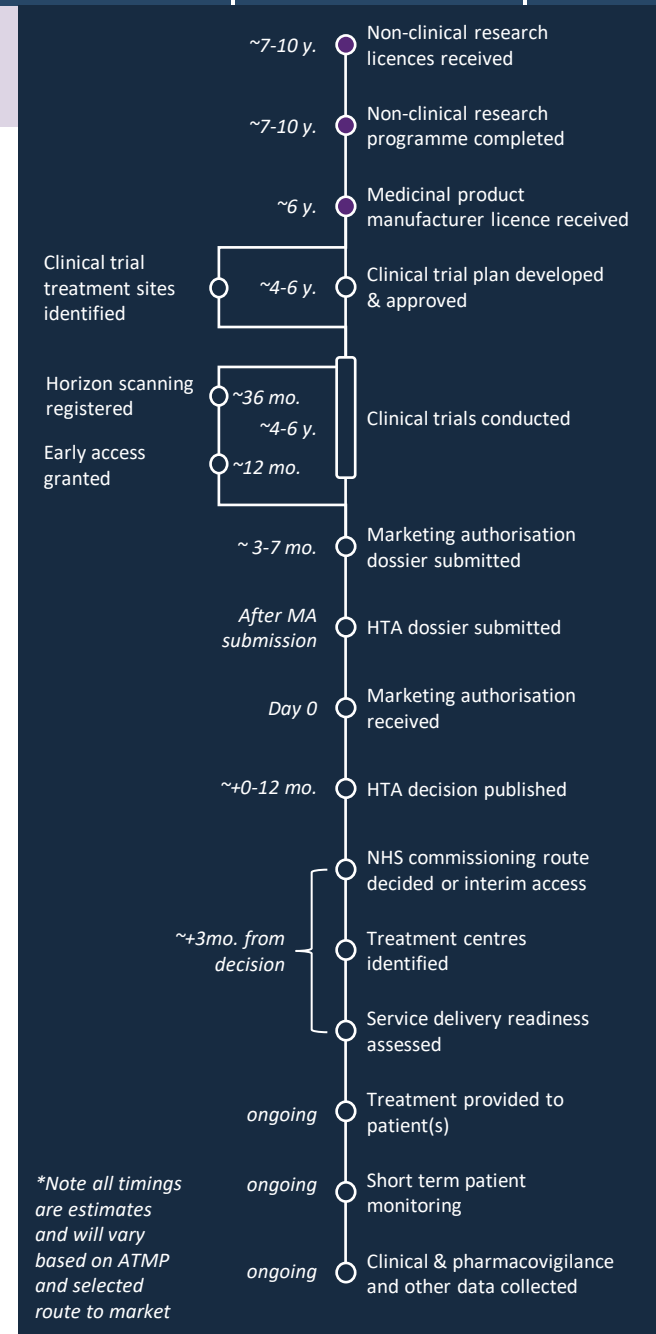
## Overview

- Consultation with patient groups through Patient and Public Involvement is becoming increasingly important and may be considered as a key element in every developer's clinical trial design
- Developers are advised to consider when to alert disease specific non-profit organisations supporting patients to notify them of upcoming treatments
- A Quality Management System (QMS) will be essential to a successful clinical trial
- For later stage trials, developers should consider requesting external/payer/regulator/disease clinical expert input on trial design to ensure that the evidence package will be comprehensive and meet requirements for payer assessment
- ATMP developers should ensure that considerations such as compassionate use, exit options and liability are considered as part of the trial protocol
- Assistance is available from the NIHR Office for Clinical Research Infrastructure (NOCRI) which helps charities, industry and other research funders work in partnership with NIHR – details can be found here
- The ATTC has developed a CAR T clinical trial guide for patients which may provide useful guidance for considerations during trial planning

## To-do list

## Output




**Linked steps** **Who is involved?** **Best practices & tips**

**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

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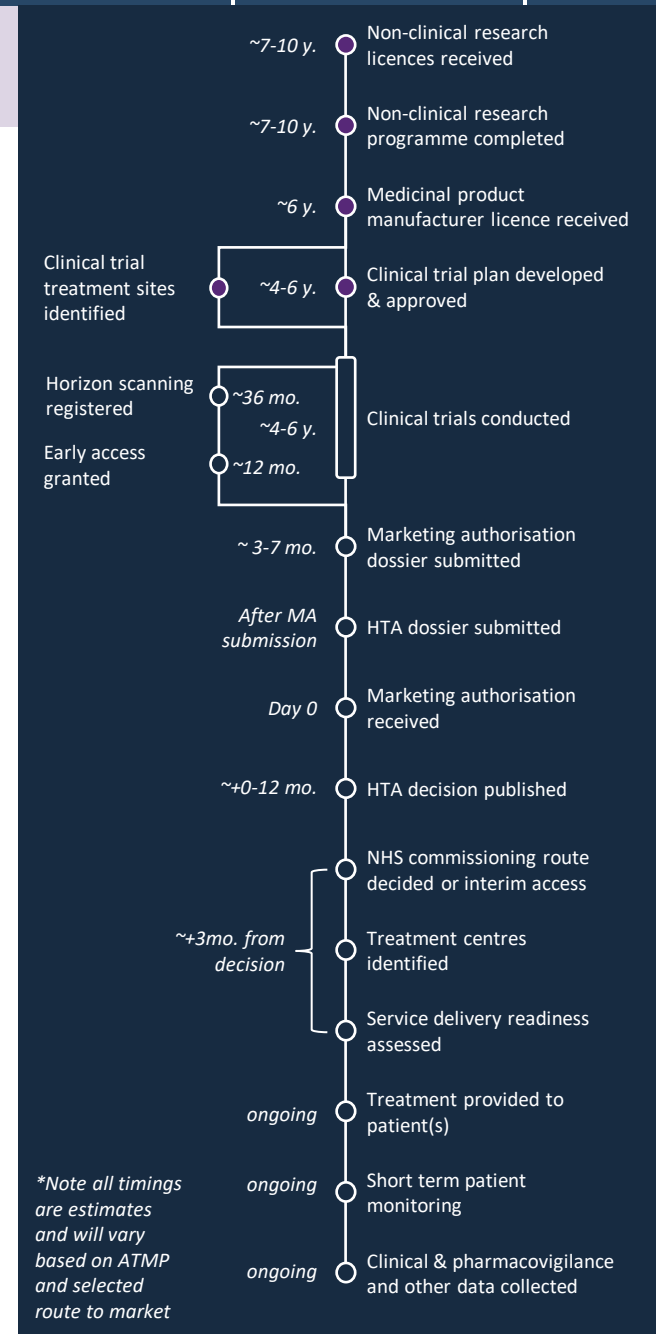
- Trial recruitment

**Overview** | To-do list | Output

Conduct process review and ensure that all processes are documented (for example, process for out of specification use in trial, process for batch release and approval, liability agreements) and confirm stakeholder awareness.

Ensure ATMP handling manuals are in place and that all relevant stakeholders involved in the trial are aware of and have reviewed the manuals. This will ensure that trial sites are prepared and that the ATMP can be delivered appropriately.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

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- Trial recruitment

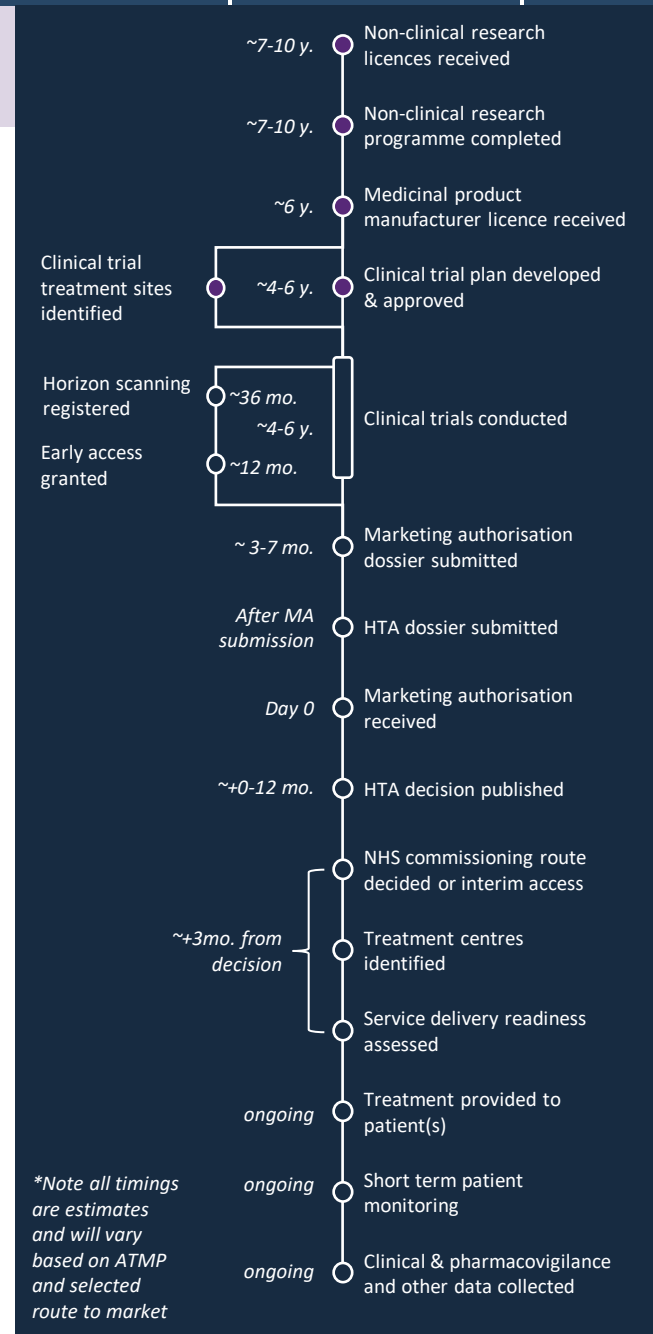
Overview | **To-do list** | Output

- Conduct process review
  - Review GMP requirements here and ensure that batch release and approval and out of specification processes are compliant
  - Review guidance from the National Institute for Biological Standards and Control (NIBSC) on batch release in the UK here
  - Review SPS out of specification ATMP guidance here
- Ensure processes are documented and circulate process documentation and handling manuals to clinical trial site staff

### When

Prior to commencement of clinical trials

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

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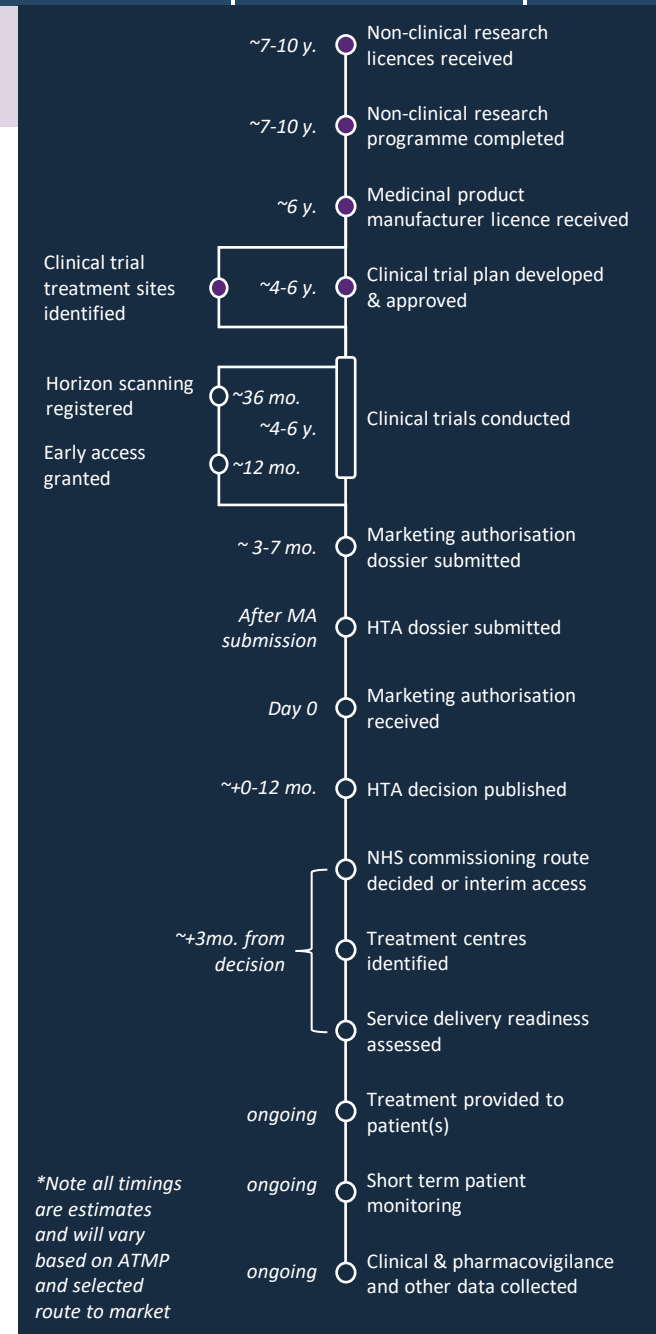
## Overview

- Process documentation
- ATMP handling manuals
- Clinical trial site staff awareness

## To-do list

## Output




**Linked steps** | **Who is involved?** | **Best practices & tips**

**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

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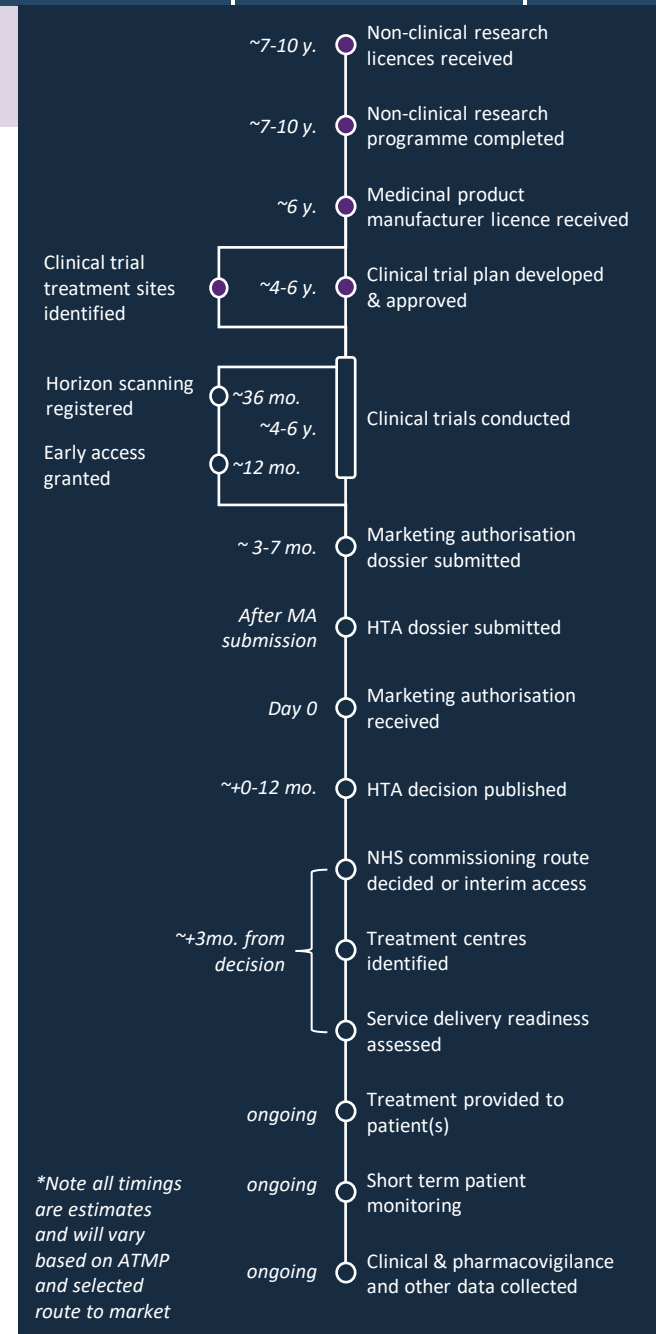
## Overview

## To-do list

## Output

GxP compliance & certification

**Linked steps** **Who is involved?** **Best practices & tips**



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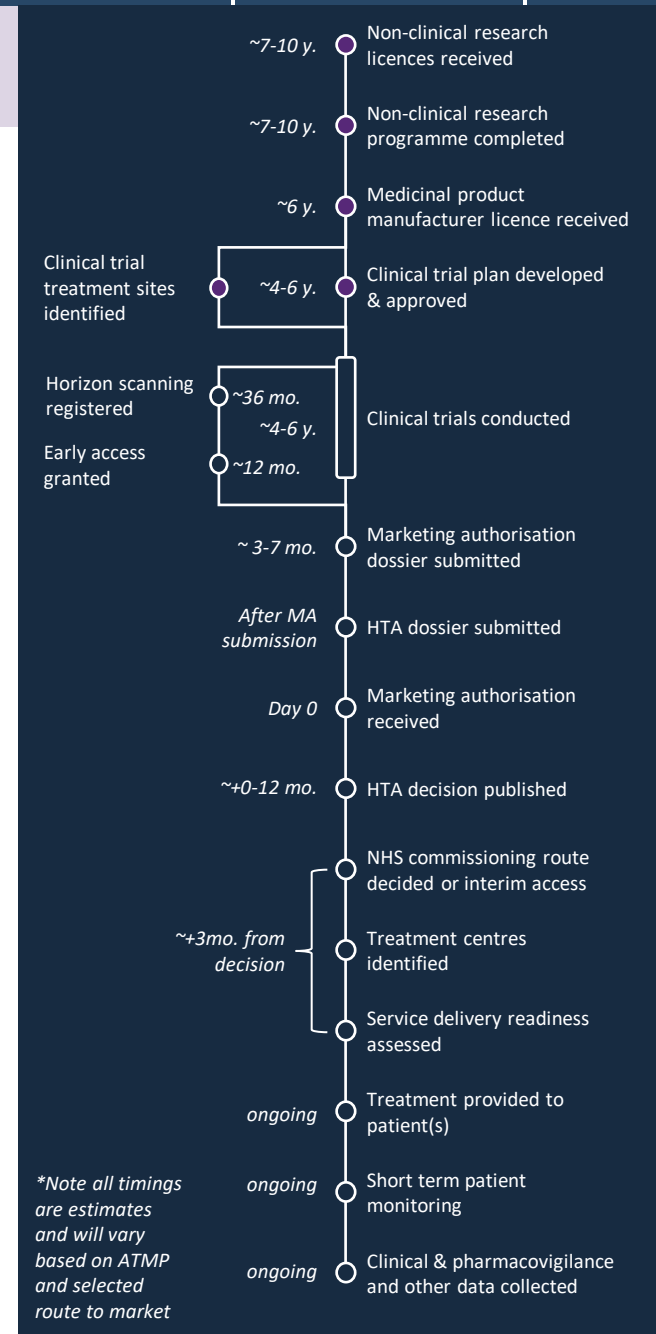
## Overview

- ATMP developer
- Clinical trial site stakeholders (e.g. pharmacy)

**Linked steps** | **Who is involved?** | **Best practices & tips**

## To-do list

## Output



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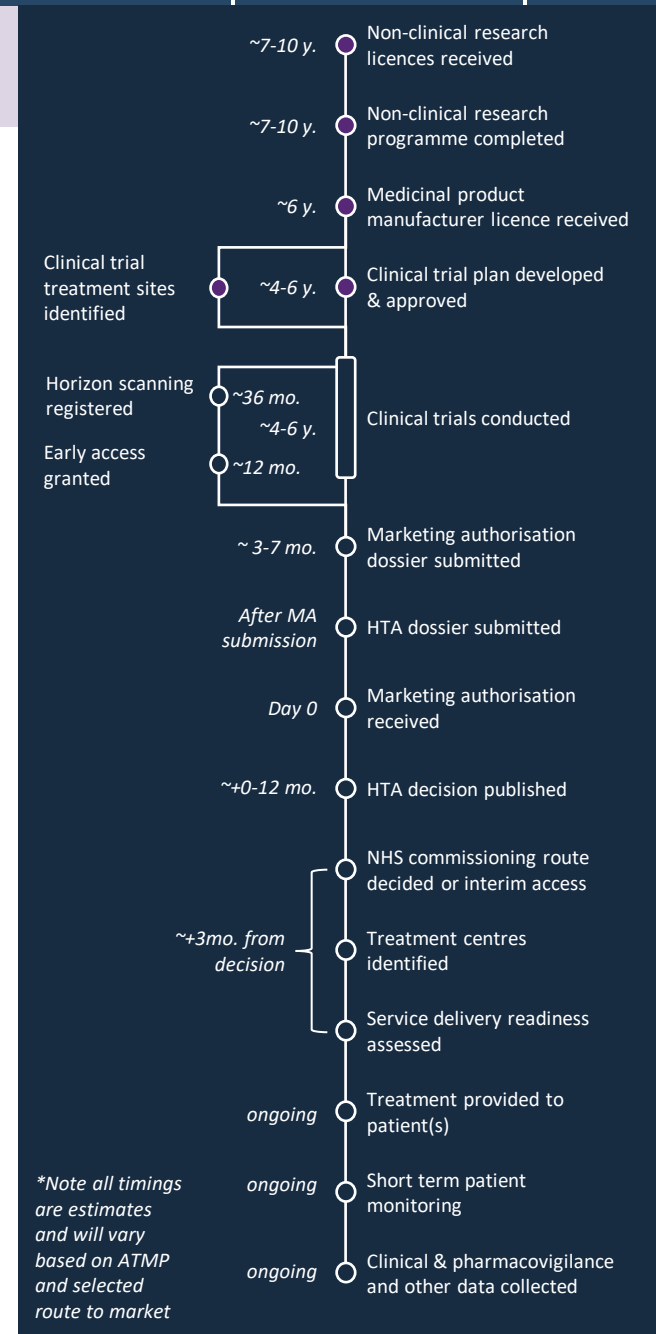
## Overview

## To-do list

## Output

- It is important to think about the end-user when tailoring processes during a clinical trial. Developers should consider existing NHS infrastructure and that which is likely to be available at launch to ensure a smooth post-authorisation implementation
- Review governance preparation guidance for gene therapies from the Pan UK Pharmacy Working Group here

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

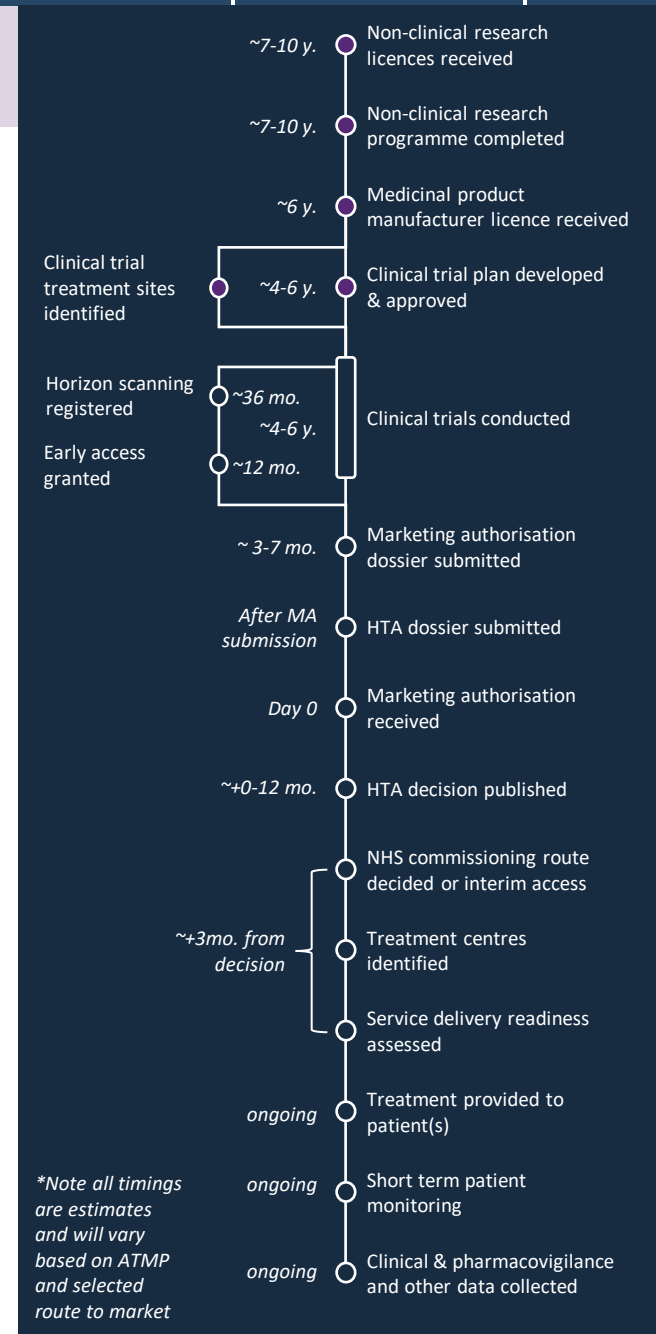


**Overview** | To-do list | Output

All clinical trials require documentation on informed consent. Informed consent must be obtained for each trial participant. The proposed informed consent documentation will need to be included for approval by research ethics committees.

When developing informed consent procedures, developers are advised to involve relevant patient groups for co-development. Documentation of this must be included in the dossier for ethics approval as part of the clinical trial application.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



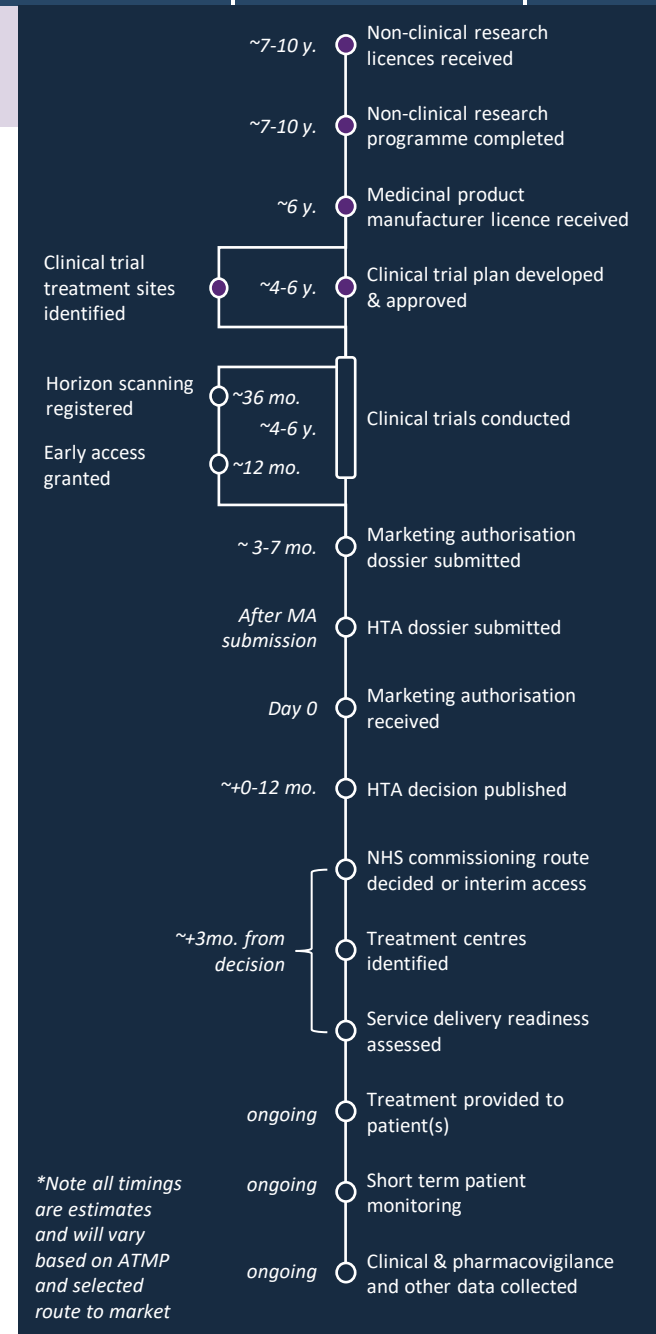
Overview | **To-do list** | Output

- Review guidance on developing informed consent procedures here
- Review NHS Health Research Authority resources here
- Review and test informed consent procedures with relevant patient and public groups to ensure they are fit for purpose
- NIHR resources on patient & public involvement (PPI) can be found here

**When**

Prior to clinical trial application

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

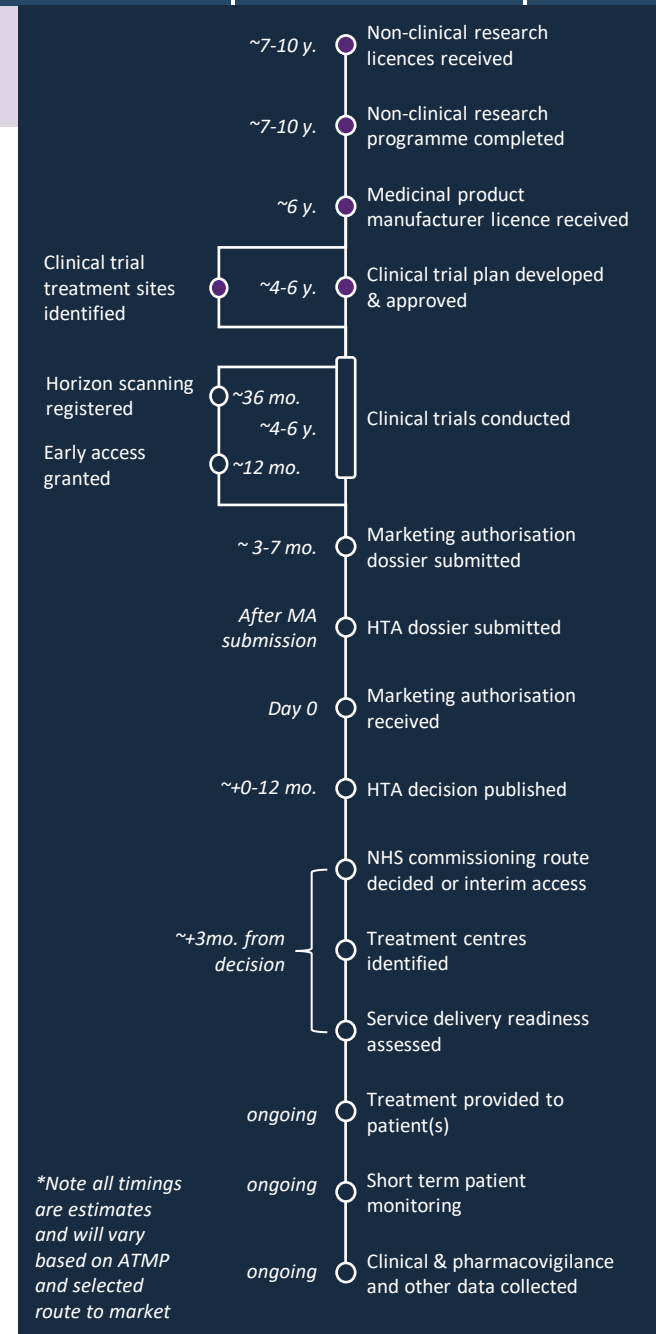
## KEY TOPICS



Overview | To-do list | **Output**

- Informed consent procedures to be included in ethics submission via Integrated Research Application System (IRAS)

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

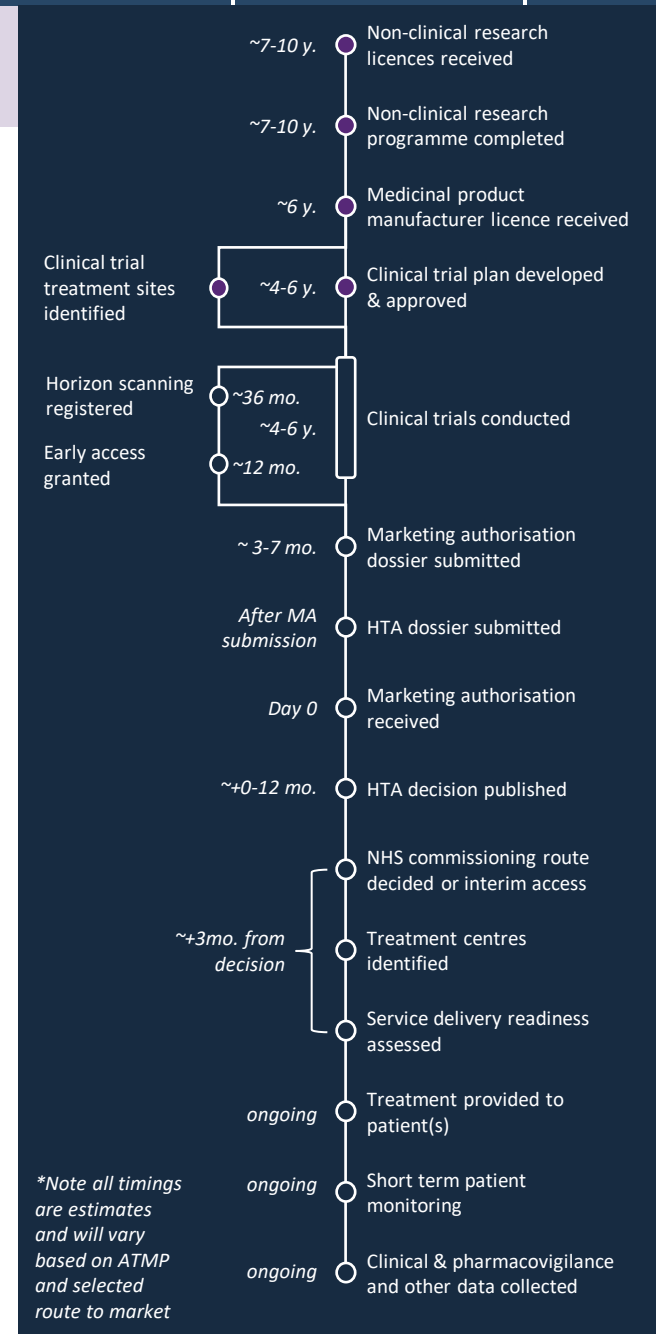
## To-do list

## Output

Regulatory and/or scientific advice

Clinical trial planning, design and protocol development

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- GxP compliance & certification
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- **Informed consent procedure development**
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

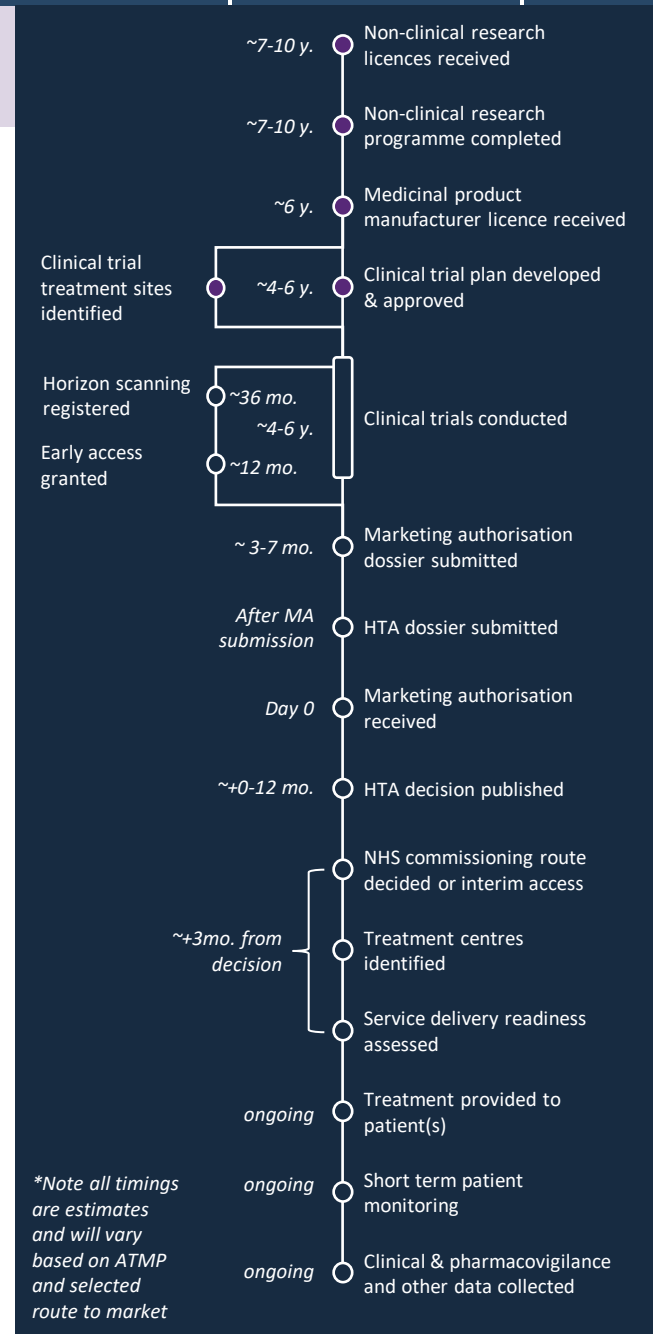
## Overview

## To-do list

## Output

- ATMP developer
- Patient groups

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

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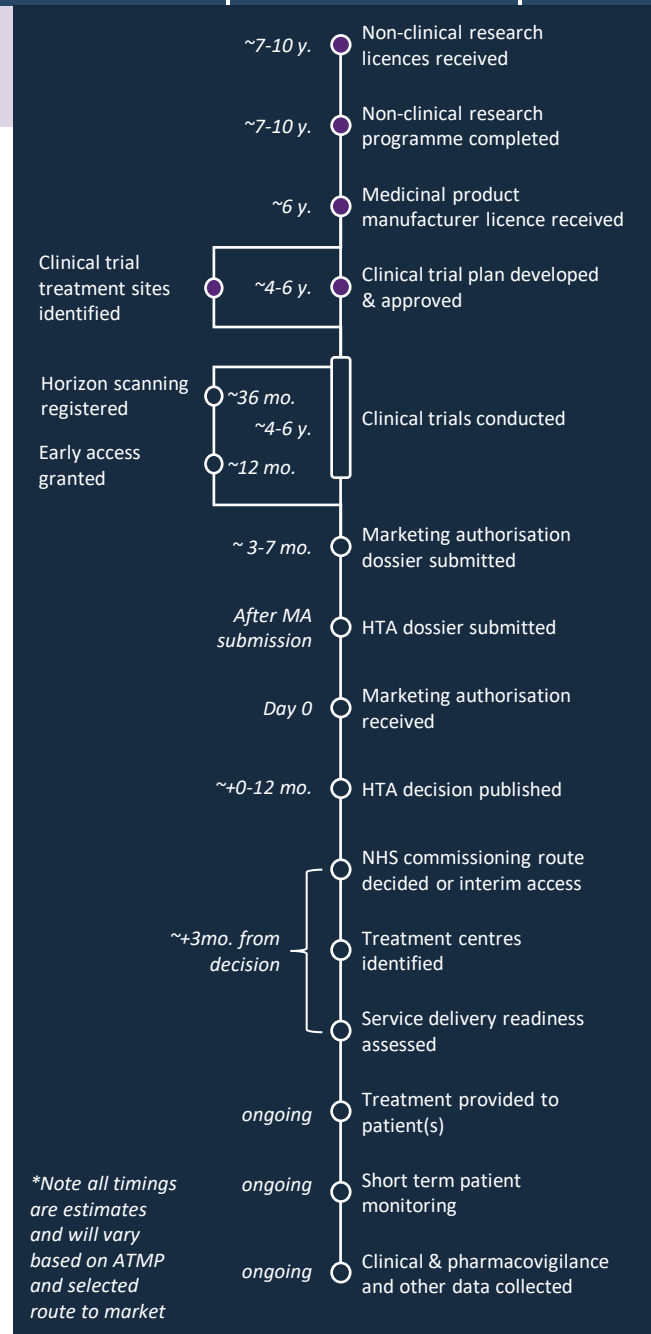
## Overview

## To-do list

## Output

- Developers should consider involving PPI at an early stage in the development of the informed consent procedures

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

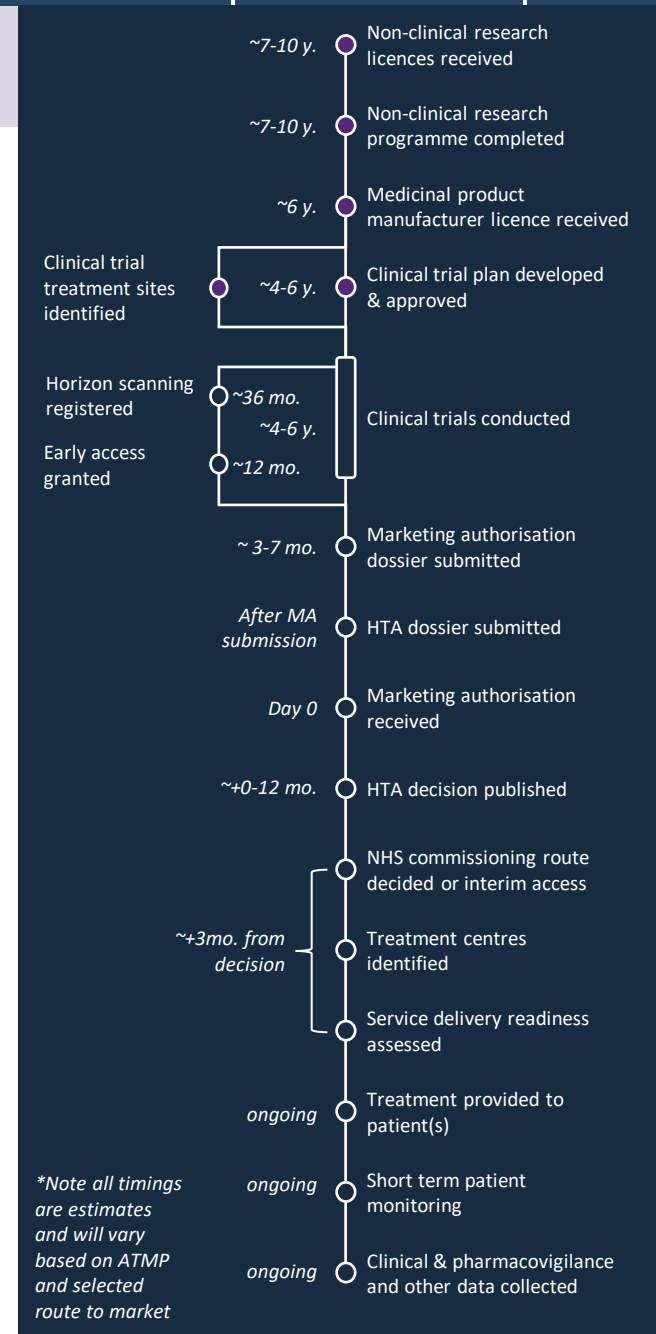


**Overview** | To-do list | Output

Developers must register their clinical trial on a publicly accessible database and generate a Trial number for inclusion in their Clinical Trial Application.

For UK only trials, established international registers such as ISRCTN registry, or ClinicalTrials.gov may be used. For clinical trials with EU/EEA sites, trials must be recorded on the EU Clinical Trials Register.

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



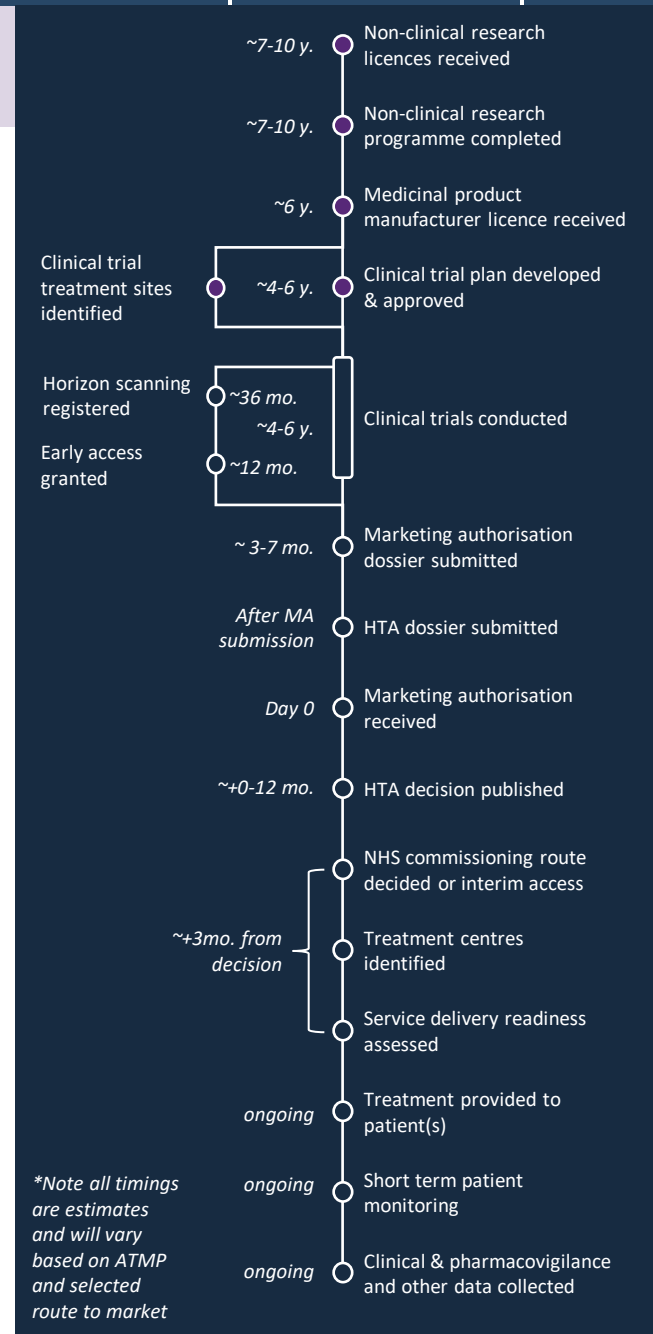
Overview | **To-do list** | Output

- Register clinical trial on publicly accessible database
  - Register the trial on ISRCTN registry here
  - See guidance on registering a trial on ClinicalTrials.gov here
  - See guidance on registering a trial on EudraCT here
- Generate Trial number via IRAS

**When**

No later than six weeks after recruitment of the first participant for the clinical trial

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

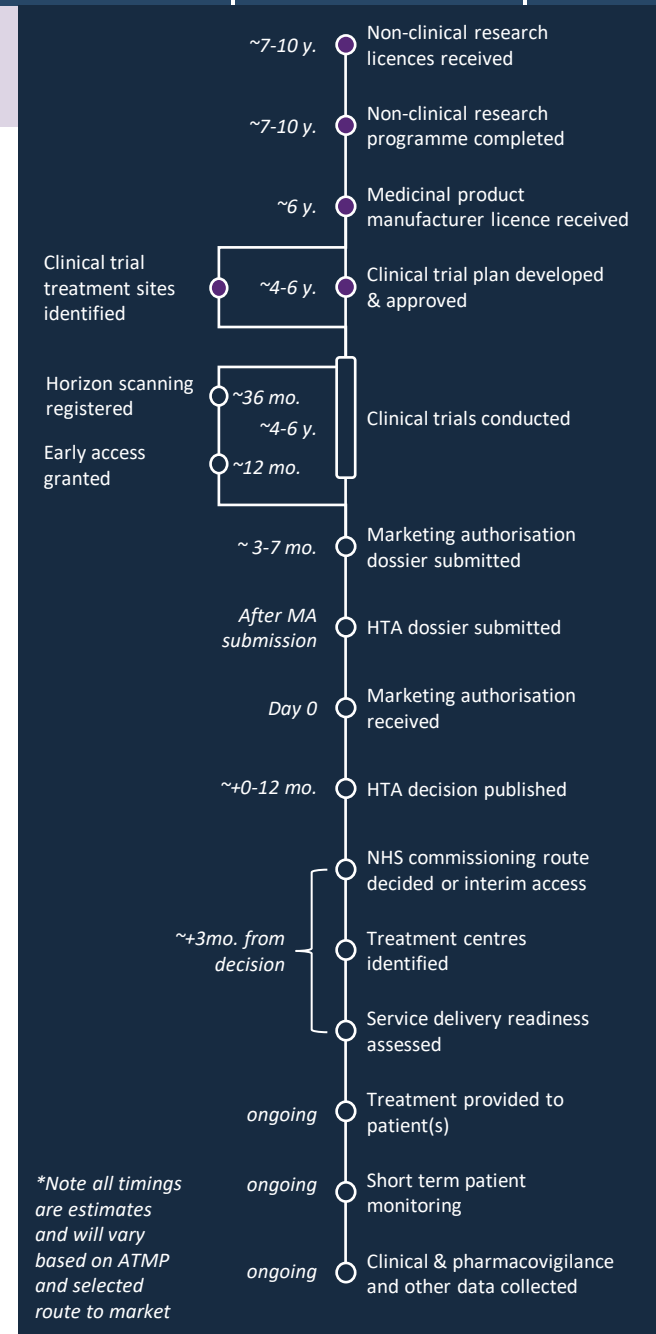
## KEY TOPICS



Overview | To-do list | **Output**

- Clinical trial registration on relevant database
- Trial number

**Linked steps** **Who is involved?** **Best practices & tips**



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- Trial recruitment

## Overview

## To-do list

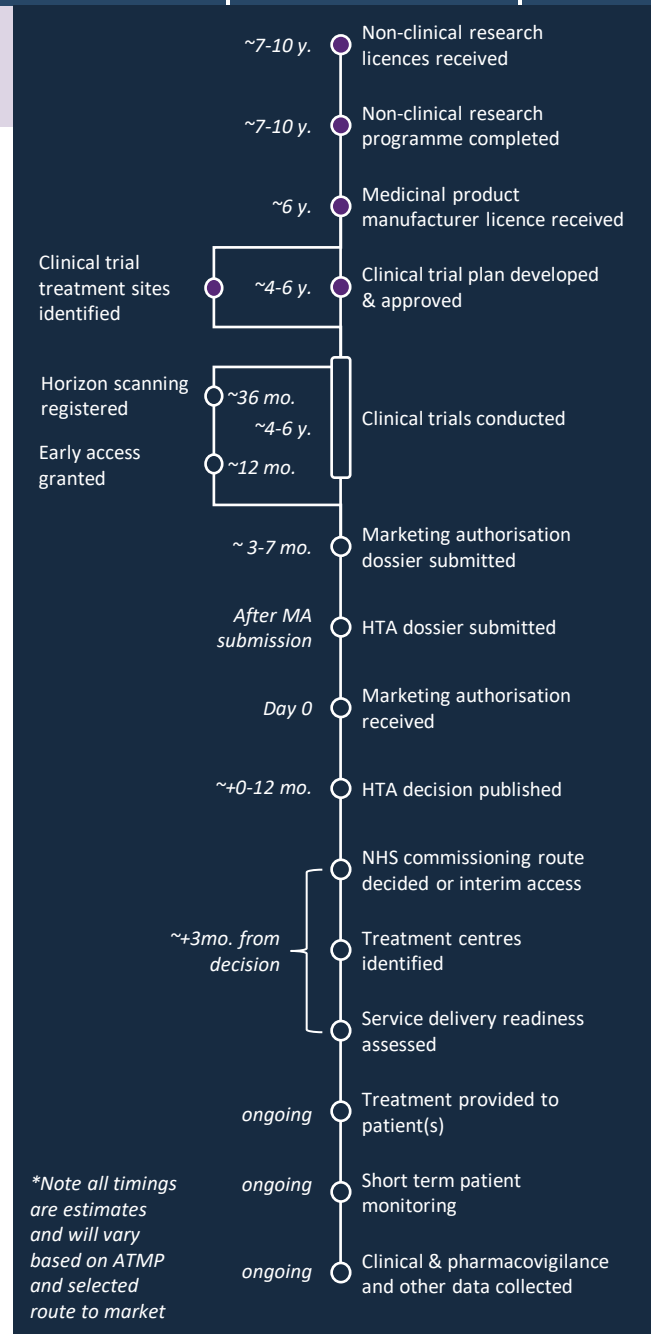
## Output

Trial recruitment

**Linked steps**

**Who is involved?**

**Best practices & tips**



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- Informed consent procedure development
- **Clinical trial registration**
- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

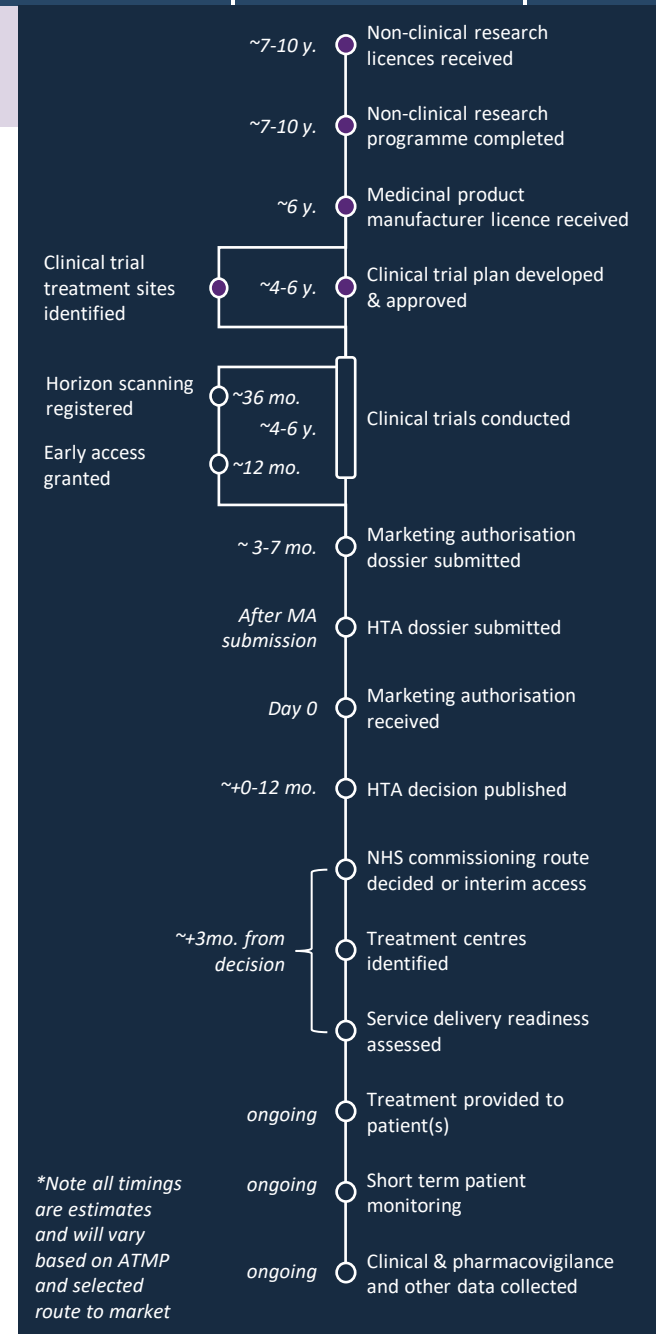
## Overview

## To-do list

## Output

- ATMP developer
- Clinical Trial databases

**Linked steps** **Who is involved?** **Best practices & tips**



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- Clinical trial authorisation
- Research documentation consolidation
- Trial recruitment

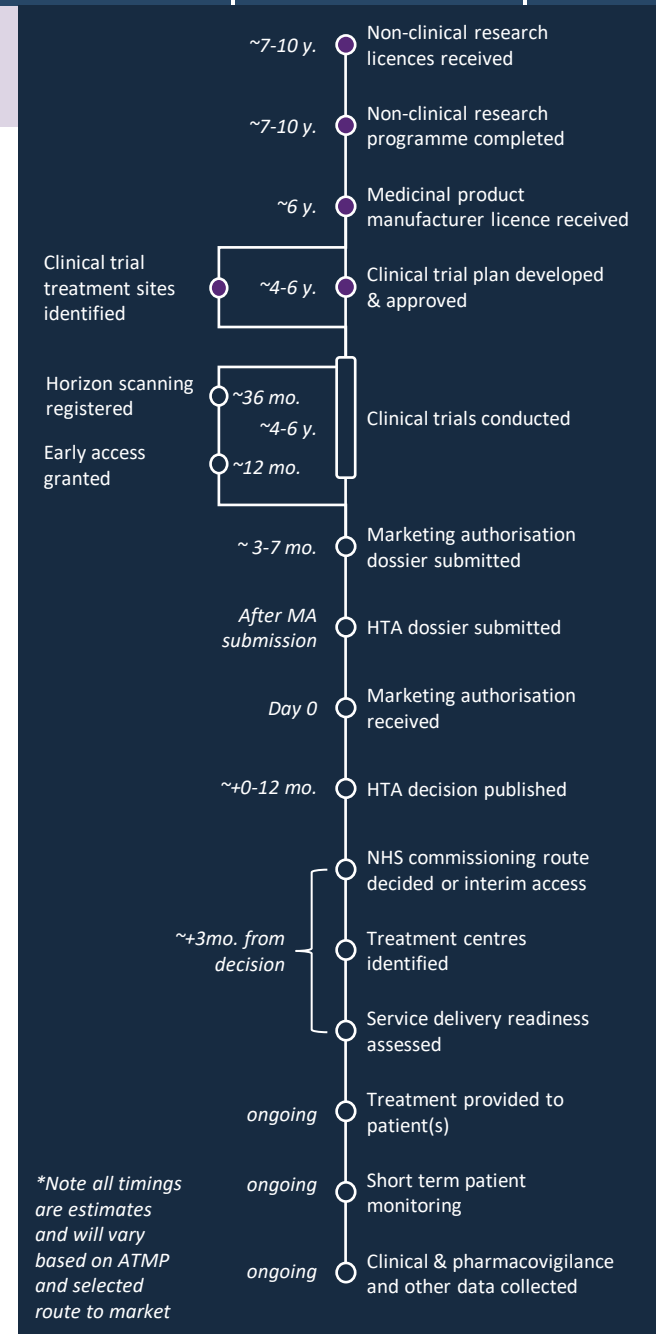
## Overview

- Best practice is to complete these steps prior to trial recruitment, and this must be no later than six weeks after recruitment of the first participant (unless the study qualifies for deferral)

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

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## KEY TOPICS

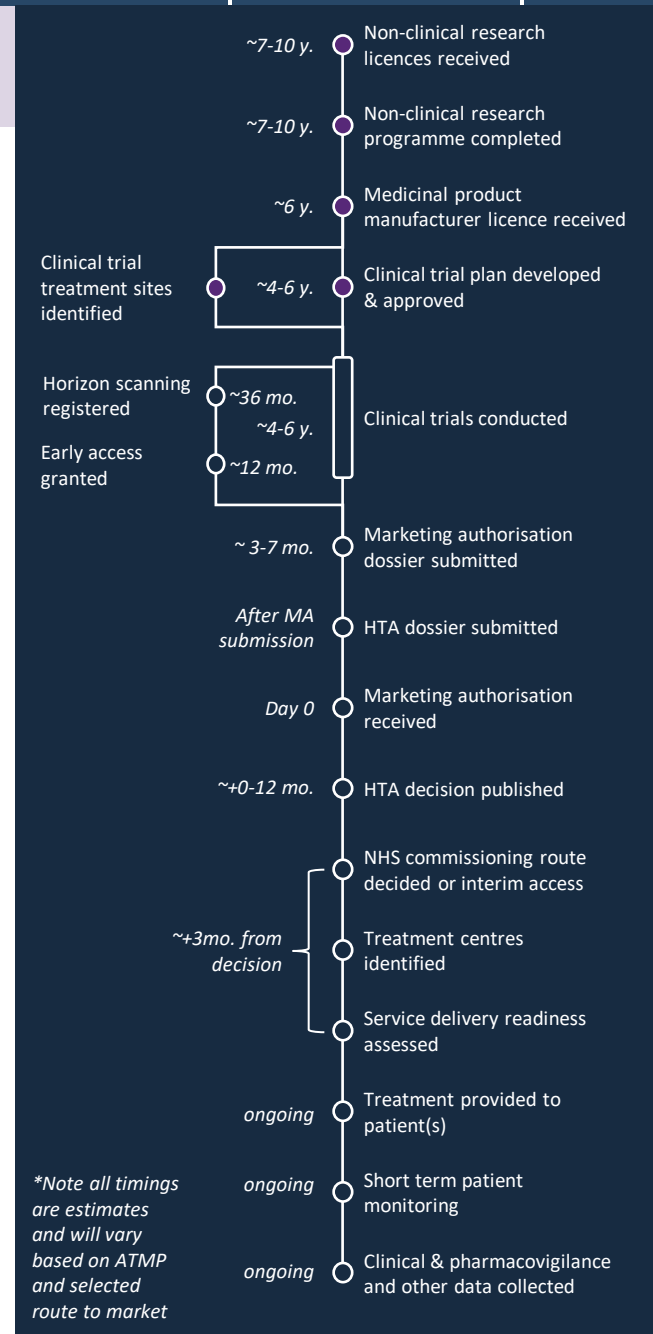


**Overview** | To-do list | Output

Developers should submit their clinical trial authorisation (CTA) application and their Research Ethics Committee (REC) or Gene Therapy Advisory Committee (GTAC) submission through the new Joint Review Service hosted by the Health Research Authority (HRA). This service can be accessed through the Integrated Research Application System (IRAS).
This allows for a concurrent review by the HRA and MHRA and provides a co-ordinated review process and will become mandatory for all new applications from 1 January 2022. There are fees involved for these applications.

ATMP developers should also apply for approval from their local NHS R&D Office (if conducting a trial in NHS facilities for NHS patients) for each research site.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

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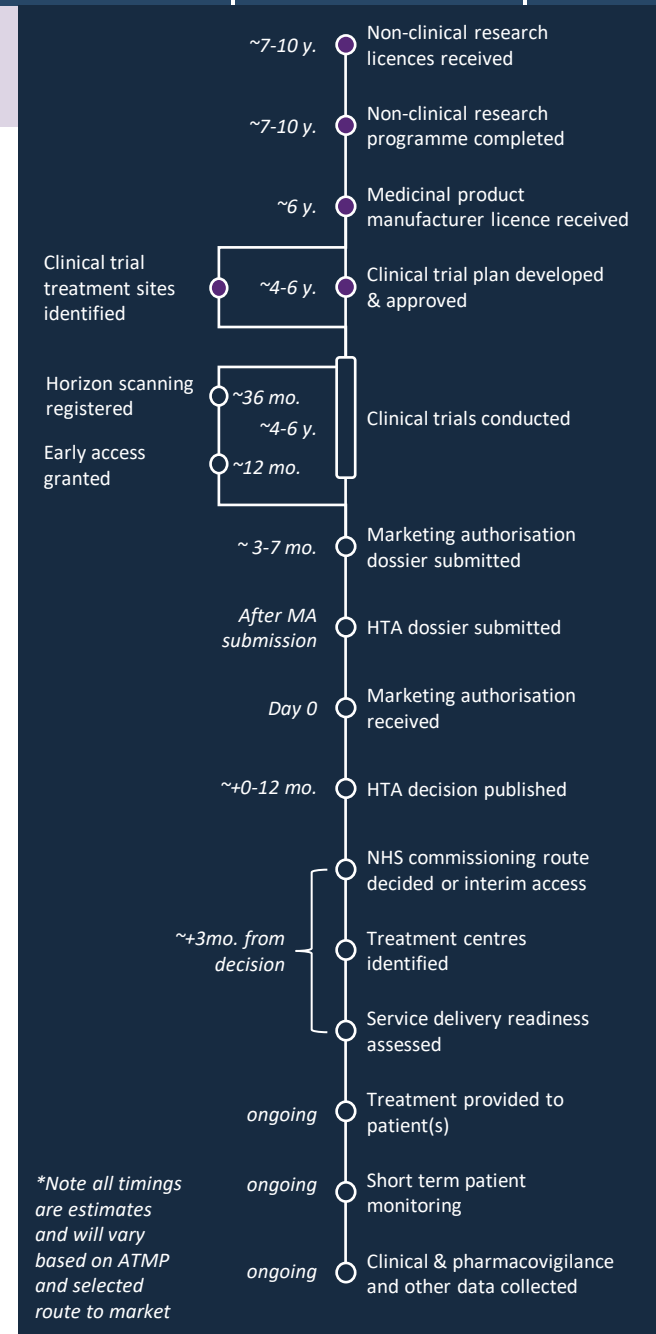
Overview | **To-do list** | Output

- Review guidance on using the combined review service for joint submission of application of clinical trial authorisation and Research Ethics Committee application here
  - A step-by-step guide can be found here
  - General guidance on clinical trial authorisation applications can be found here
- Submit joint REC & CT Application through IRAS here
  - Review information and create account with IRAS here
- Review guidance to apply for approval from the local R&D office here, all applications should be submitted via IRAS here
  - Guidance for sites in Scotland here
  - Guidance for sites in England and Wales here
  - Guidance for sites in Northern Ireland here
- Developers may be required to provide further information, any requests for this will be provided via IRAS and responses must be issued within 14 days
- A joint decision on the submission will then be provided

### When

- At time of clinical trial authorisation application
- Joint decisions from HRA (GTAC) and MHRA may have timeframes ranging from 30-90 days (depending on whether amendments are required)

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

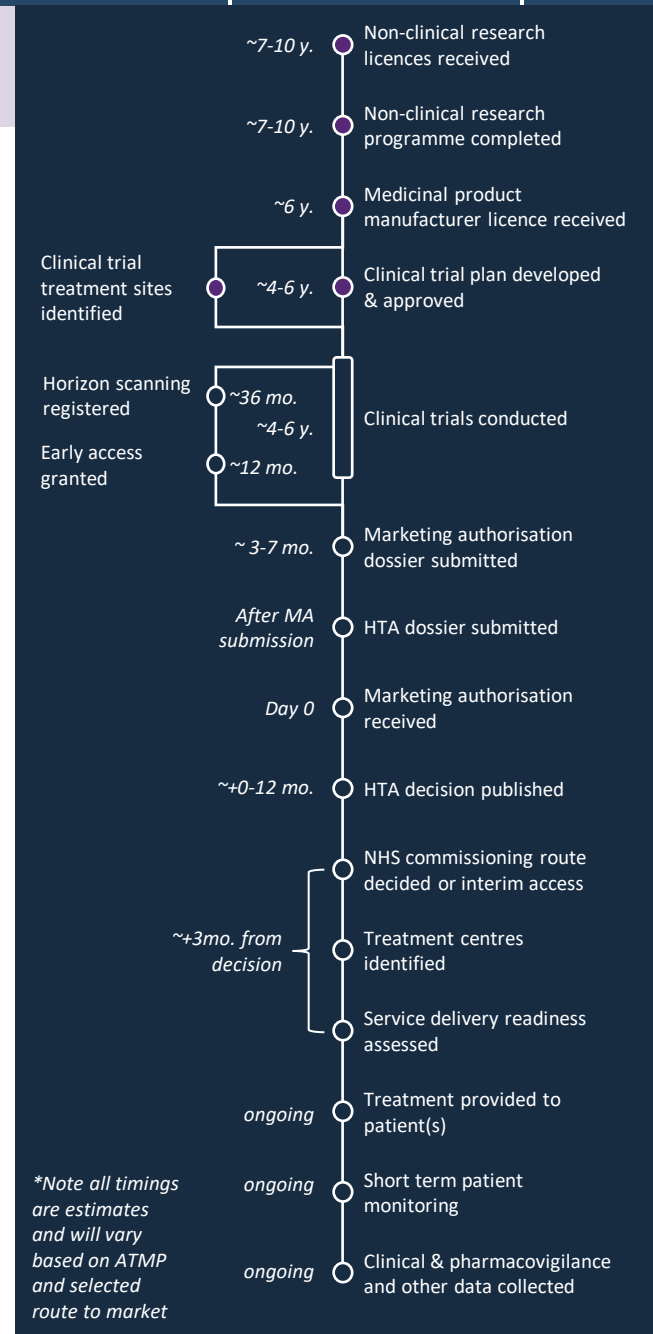
## KEY TOPICS



Overview | To-do list | **Output**

- Clinical trial authorisation
- REC Approval
- R&D Permission

**Linked steps** **Who is involved?** **Best practices & tips**



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- Research documentation consolidation
- Trial recruitment

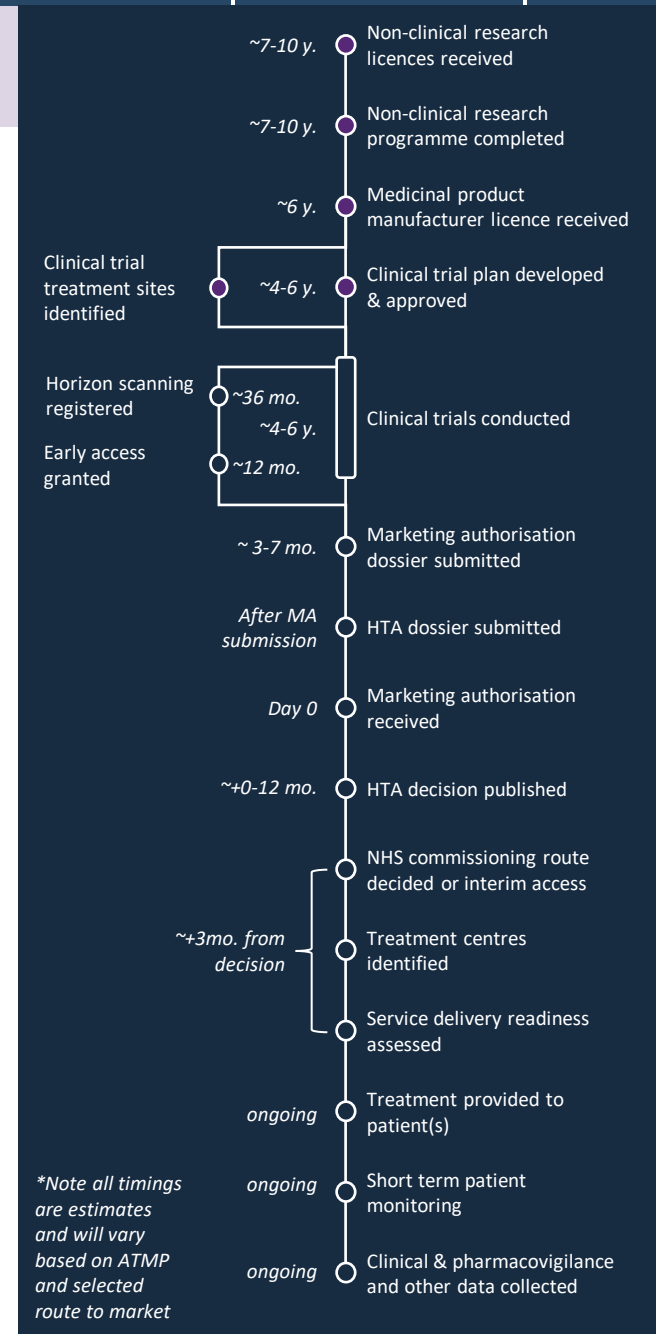
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- **Clinical trial authorisation**
- Research documentation consolidation
- Trial recruitment

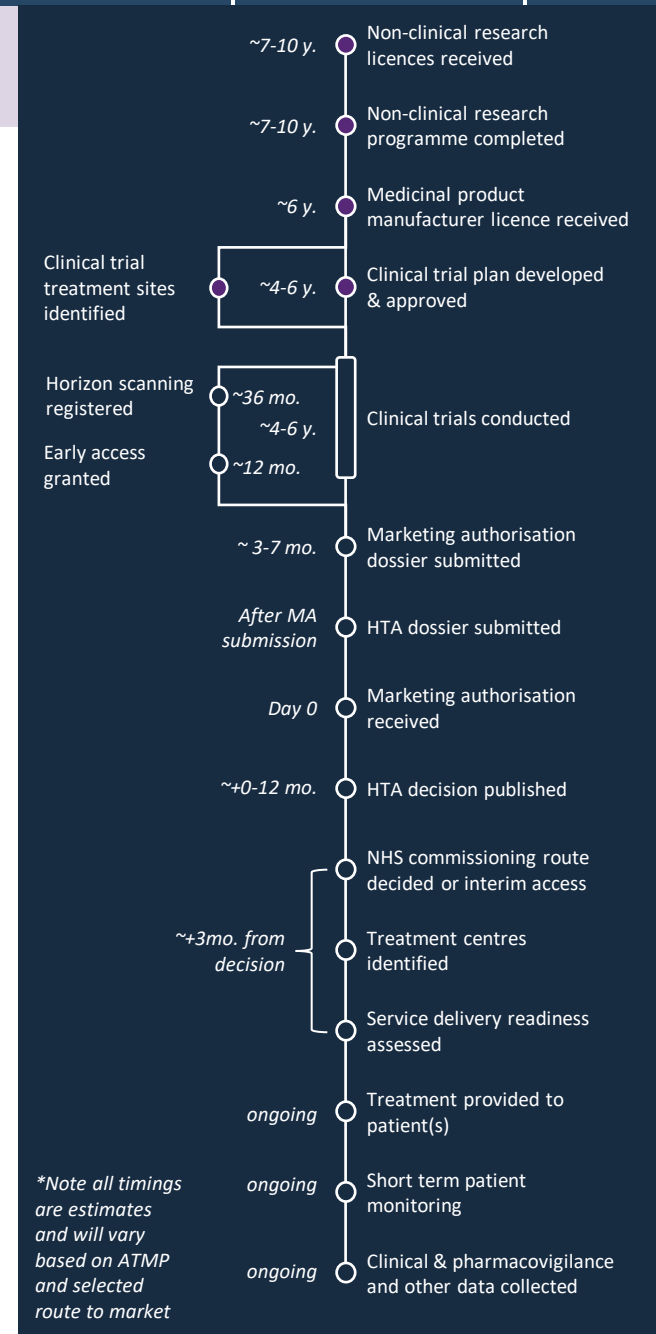
## Overview

- ATMP developer (trial sponsor)
- Principal Investigator (sometimes referred to as Chief Investigator)
- MHRA
- HRA
- NHS England & NHS across devolved nations

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- Informed consent procedure development
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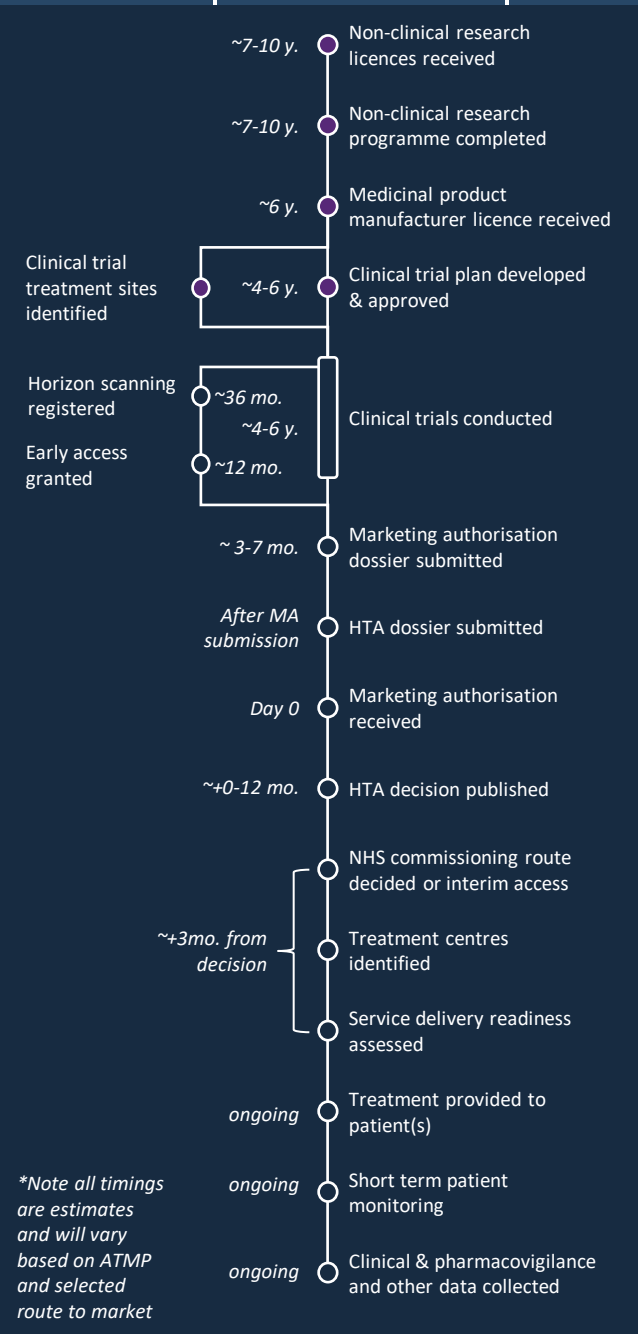
- **Clinical trial authorisation**
- Research documentation consolidation
- Trial recruitment

Overview | To-do list | Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



**Overview** | To-do list | Output

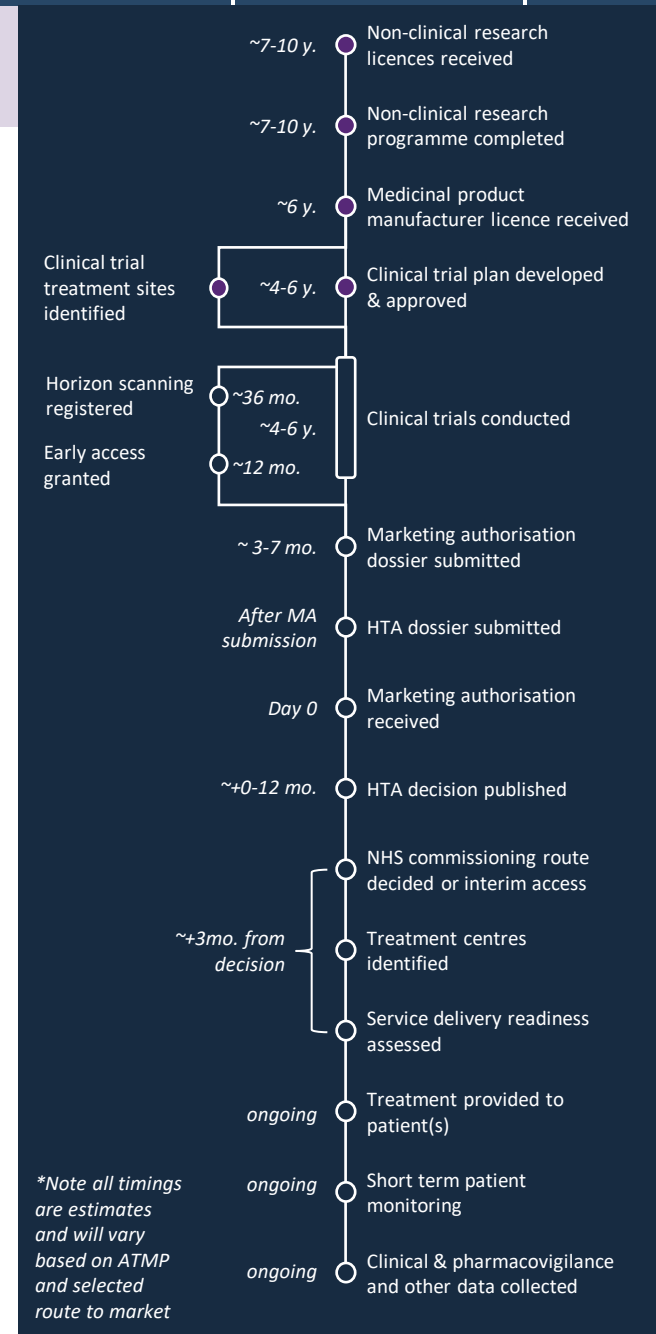
Prior to clinical trial application, ATMP developers should review the guidance documentation for conducting clinical trials in the UK and consolidate non-clinical research documentation from the non-clinical phase in preparation for their clinical trial application.

After receipt of clinical trial authorisation, ATMP developers must ensure that all of their Trial Management documentation (including documentation of approvals/authorisations) has been obtained and is version controlled.

Developers may also complete a trial document checklist to ensure that all documentation is in place.

Prior to trial recruitment, trial sponsors must be aware that trial sites must confirm that all governance processes have been completed and documented and that the site can open to recruitment.

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



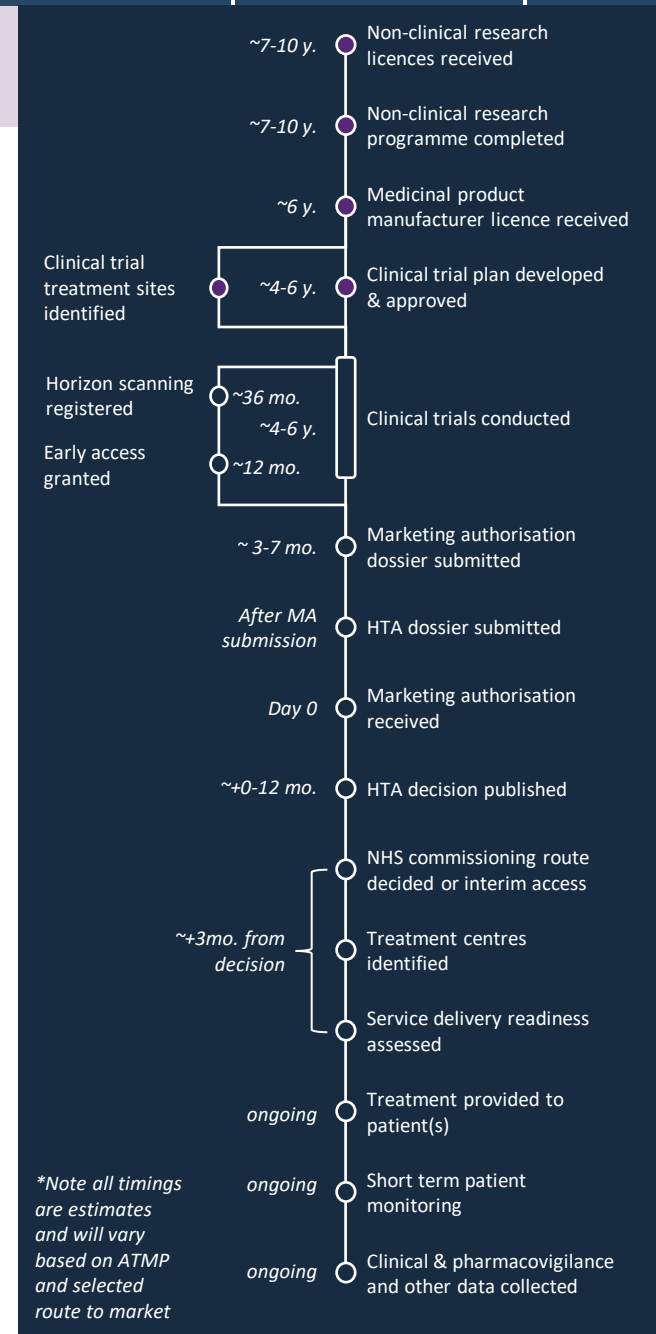
Overview | **To-do list** | Output

- General guidance on documentation required for clinical trial applications can be found here
- Further guidance including a trial document checklist can be found here

**When**

- Consolidation prior to submission of clinical trial application
- Trial management documentation checklist and ongoing management upon receipt of clinical trial authorisation

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1 What steps are required for clinical trial application?**

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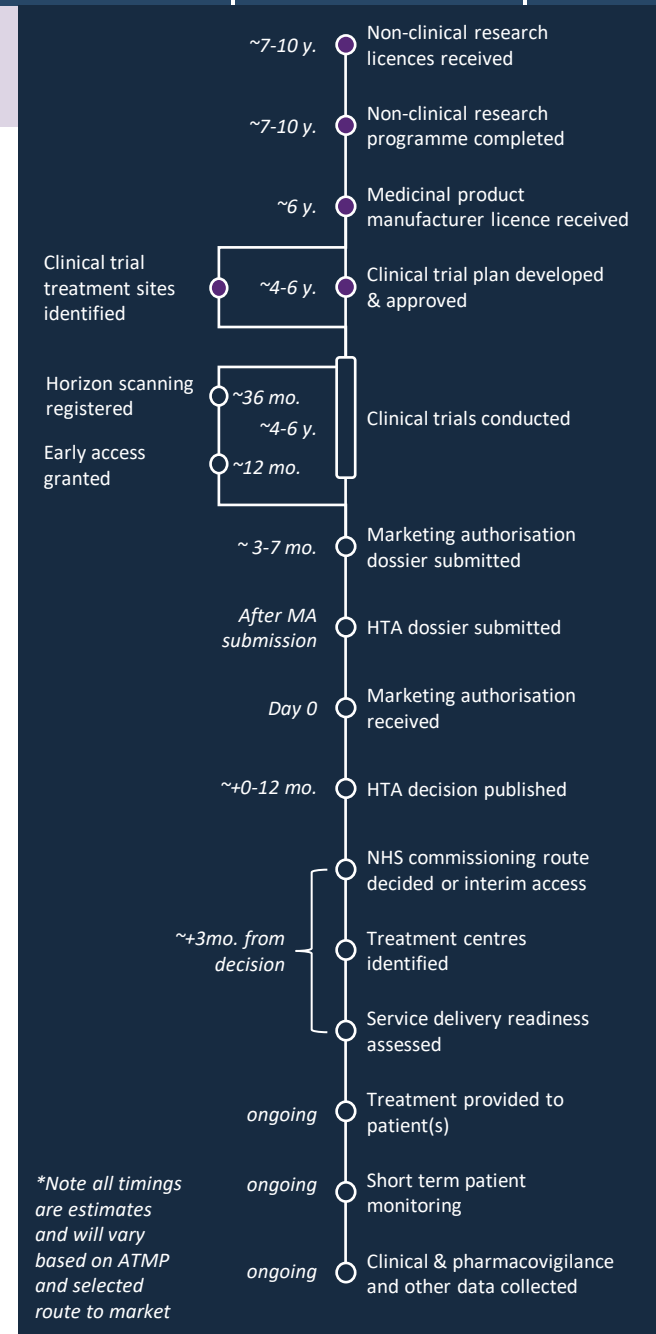
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- **Research documentation consolidation**
- Trial recruitment

Overview | To-do list | **Output**

- Trial management documentation obtained and confirmed

**Linked steps** | **Who is involved?** | **Best practices & tips**



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- Trial recruitment

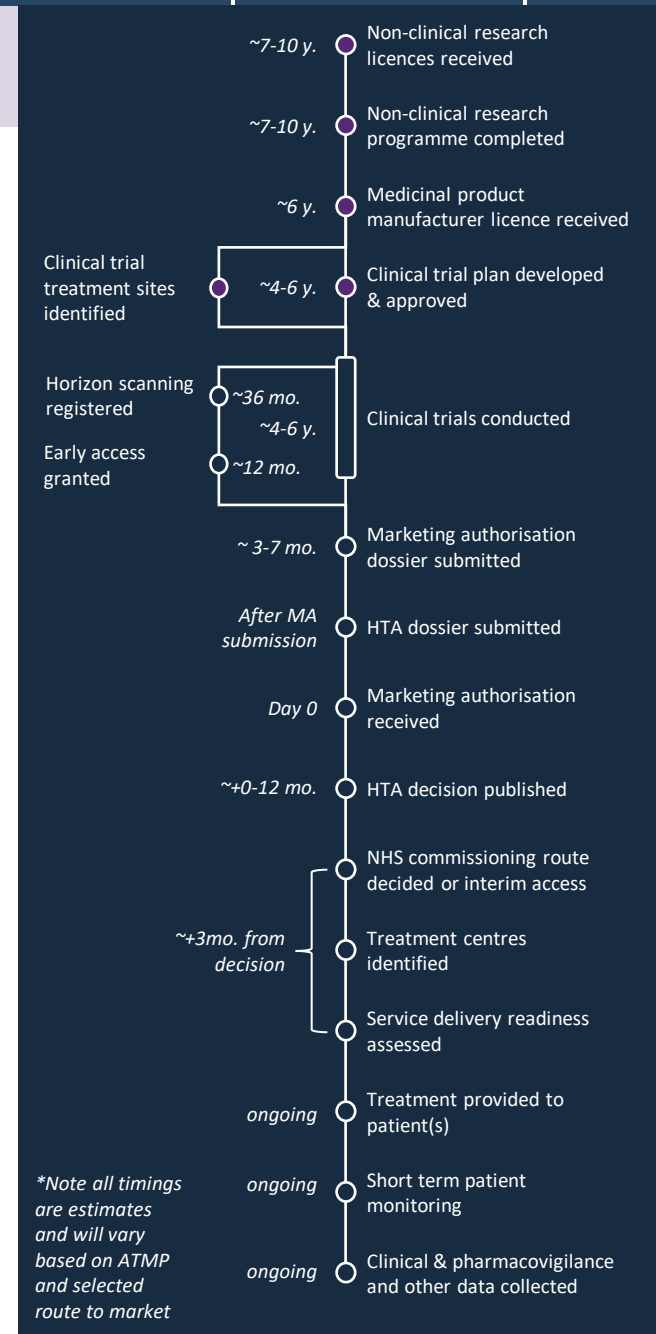
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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- Trial recruitment

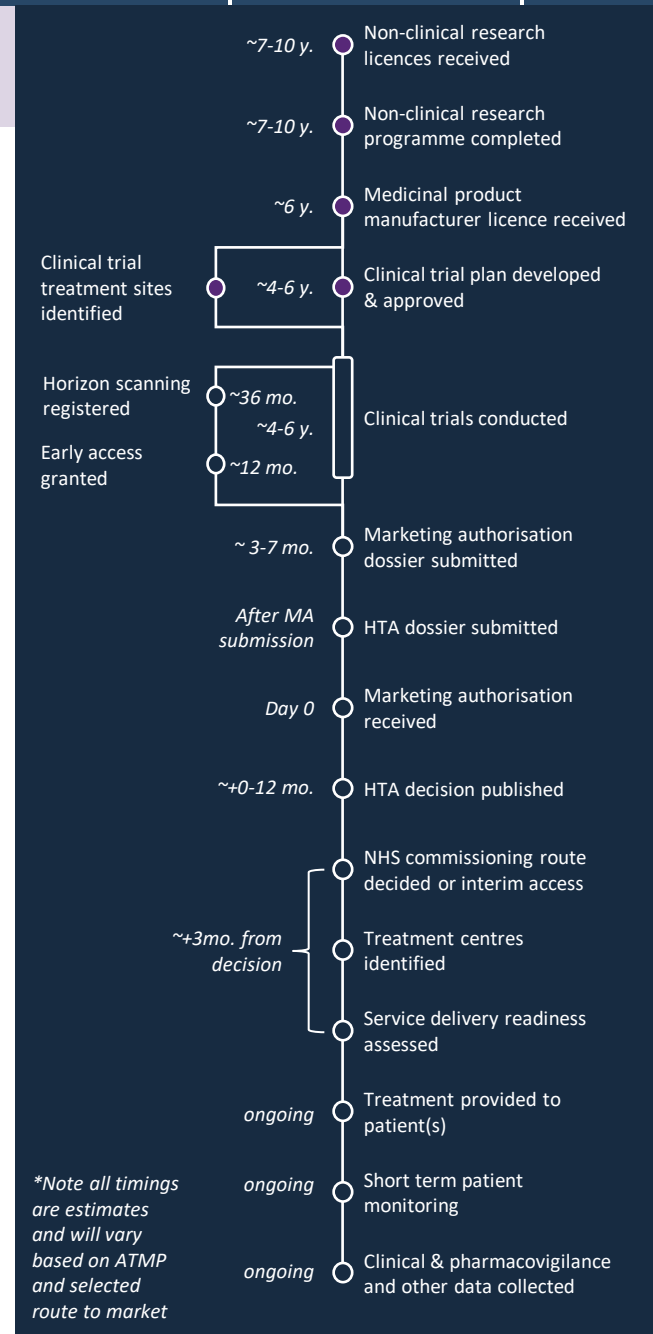
## Overview

- ATMP developer
- Trial sponsor

**Linked steps** **Who is involved?** **Best practices & tips**

## To-do list

## Output



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- Clinical trial authorisation
- **Research documentation consolidation**
- Trial recruitment

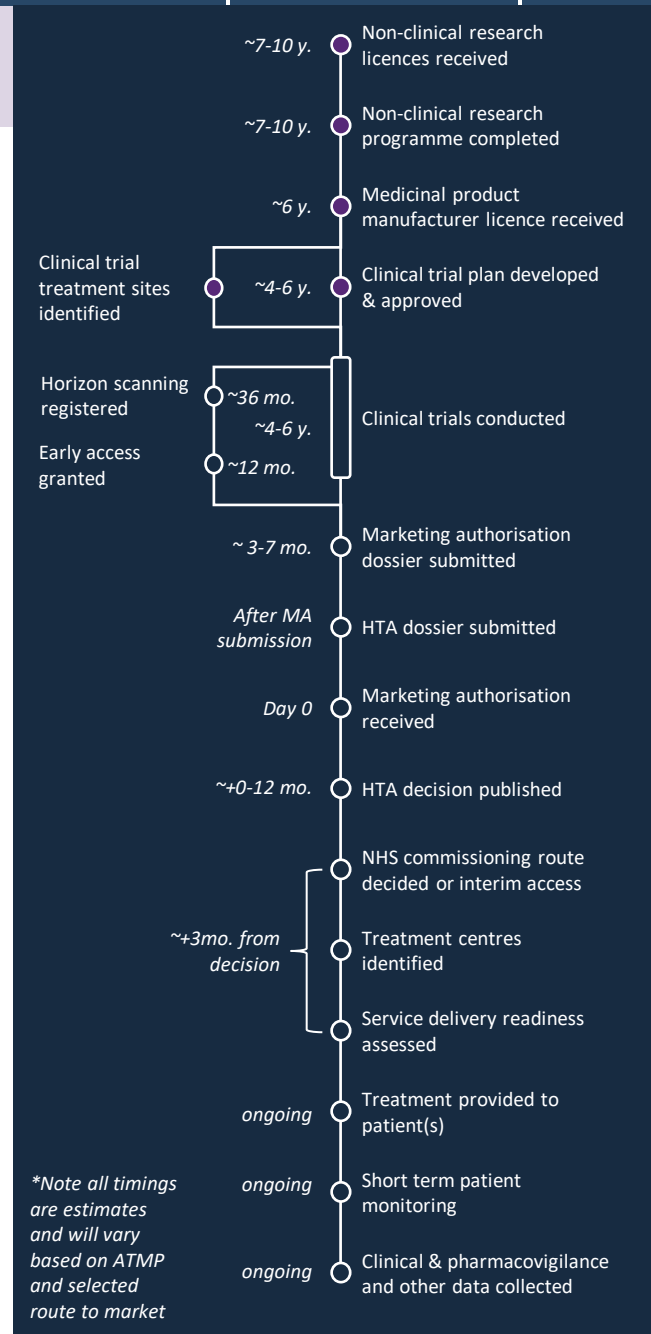
## Overview

- Ensure that ISO certified document management system is in place for technical files to facilitate file management for clinical trial application and later regulatory approval steps

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

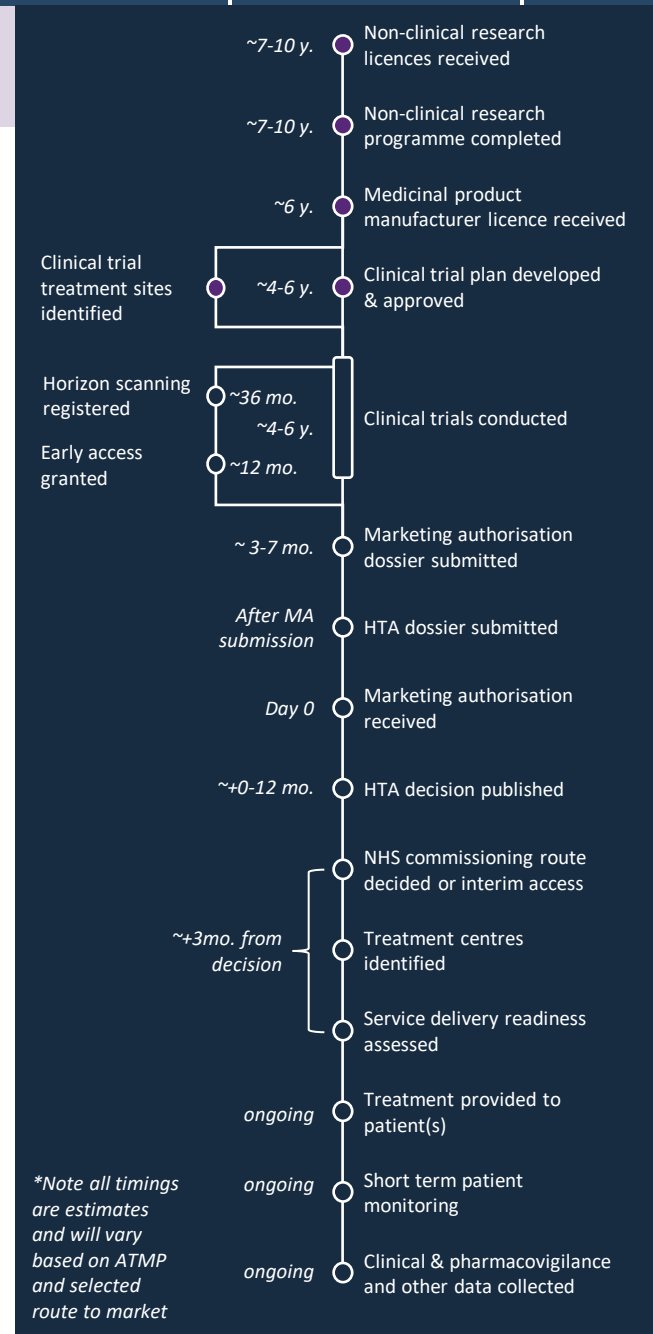


**Overview** | To-do list | Output

Once clinical trial participants have been identified, provided informed consent and have been confirmed, the clinical trial can commence (subject to completion other clinical trial application requirements).

In the event that healthy volunteers are being used in a Phase I trial, participants should be registered on The Over-Volunteering Prevention System (TOPS).

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



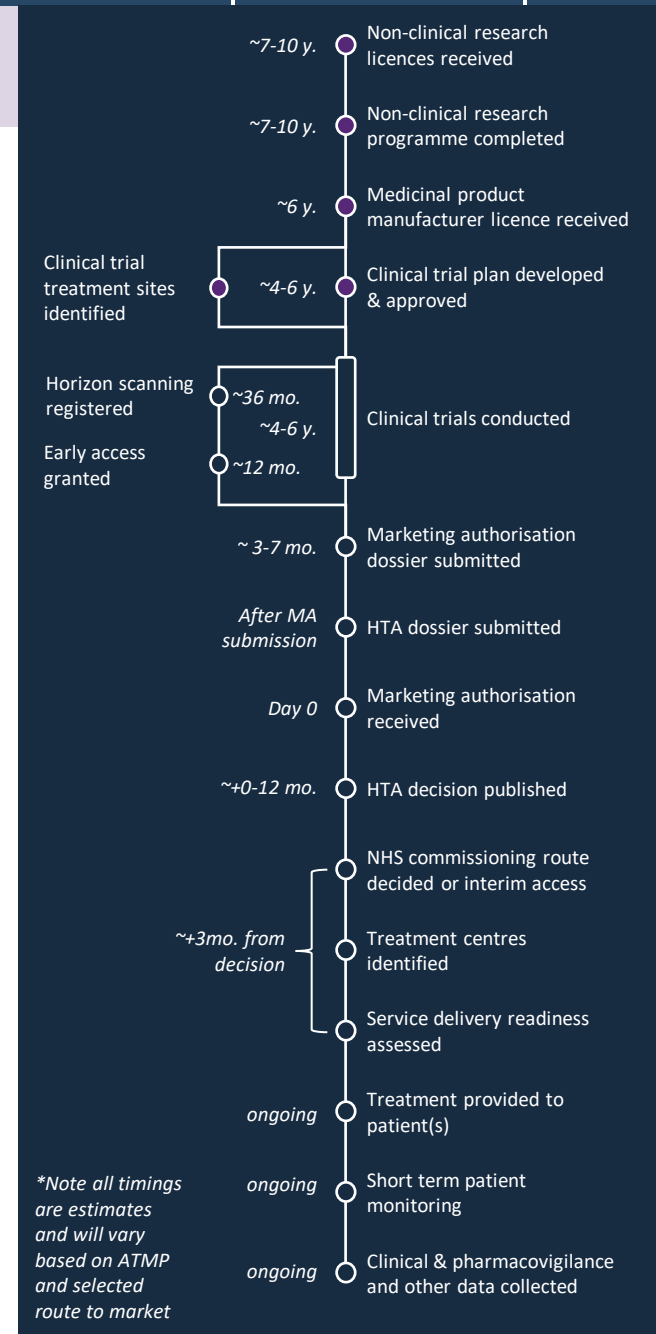
Overview | **To-do list** | Output

- Identify potential clinical trial participants
  - Consider use of National Patient Recruitment Centres if applicable for the product and research type (information here)
- Recruit trial participants
- Obtain informed consent from participants
- Register on TOPS (phase I only and only if applicable) here
- Confirm trial participants

**When**

Prior to commencement of clinical trial

**Linked steps** | **Who is involved?** | **Best practices & tips**



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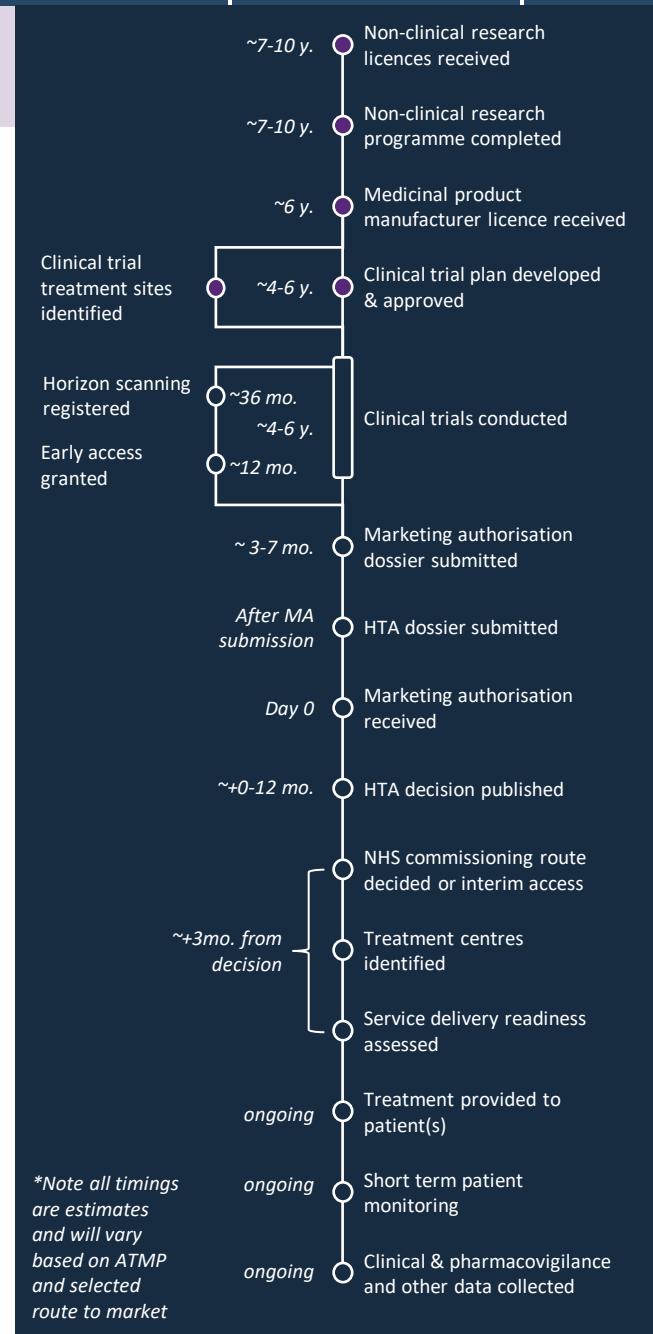
- Clinical trial authorisation
- Research documentation consolidation
- **Trial recruitment**

Overview | To-do list | **Output**

- Confirmed clinical trial participants
- Clinical trial commencement

**Linked steps** **Who is involved?** **Best practices & tips**



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## Overview

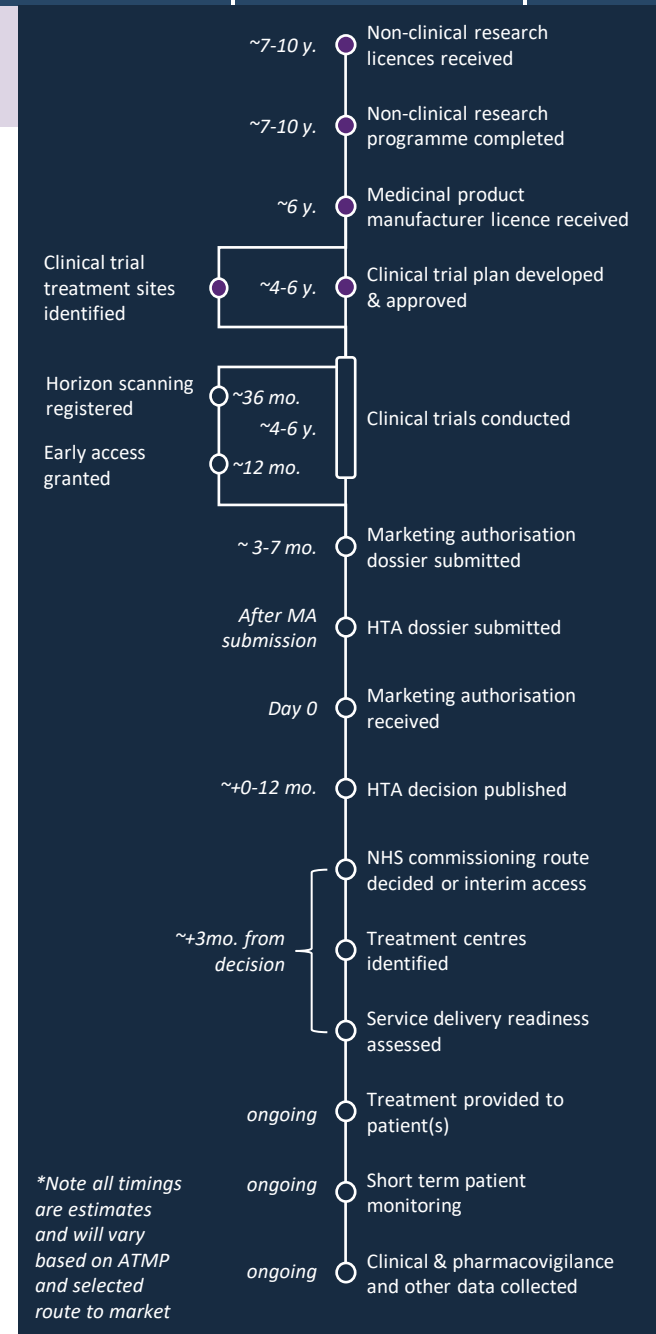
## To-do list

## Output

Informed consent procedure development

Research documentation consolidation

**Linked steps** **Who is involved?** **Best practices & tips**



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- **Trial recruitment**

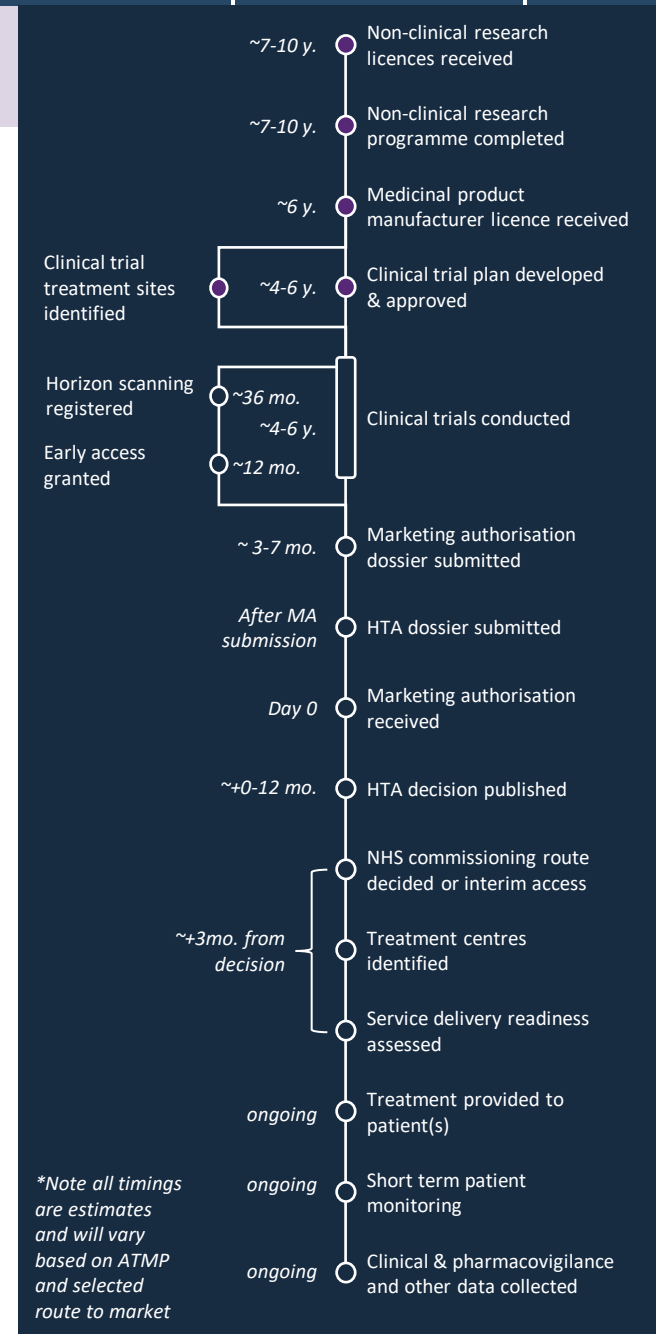
## Overview

## To-do list

## Output

- ATMP developer

**Linked steps** **Who is involved?** **Best practices & tips**



**1 What steps are required for clinical trial application?**

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- GxP compliance & certification
- Expert Advisory Group Clinical Trial Assessment [if applicable]
- Clinical trial planning, design & protocol development
- Governance & process documentation
- Informed consent procedure development
- Clinical trial registration
- Clinical trial authorisation
- Research documentation consolidation
- **Trial recruitment**

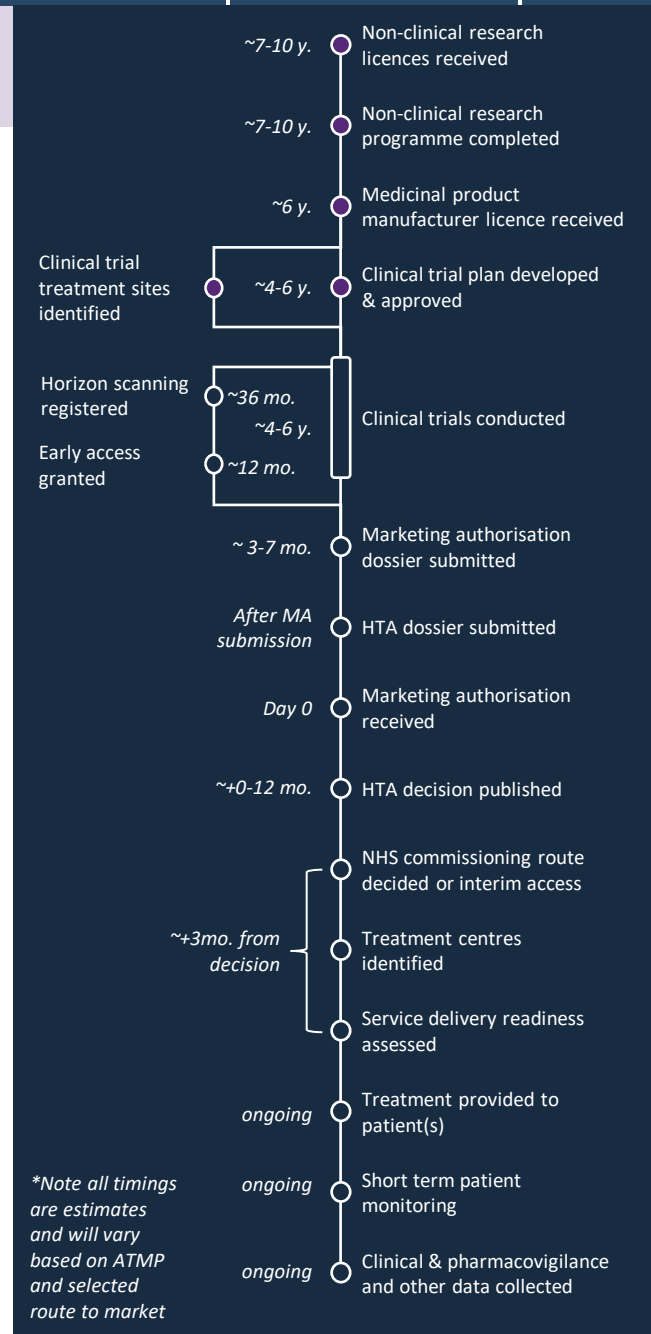
## Overview

- The often small target populations of ATMPs can make clinical trial participant recruitment difficult and may take longer than for conventional trials, therefore early engagement to identify potential trial participants is advised

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

**Overview** | To-do list | Output

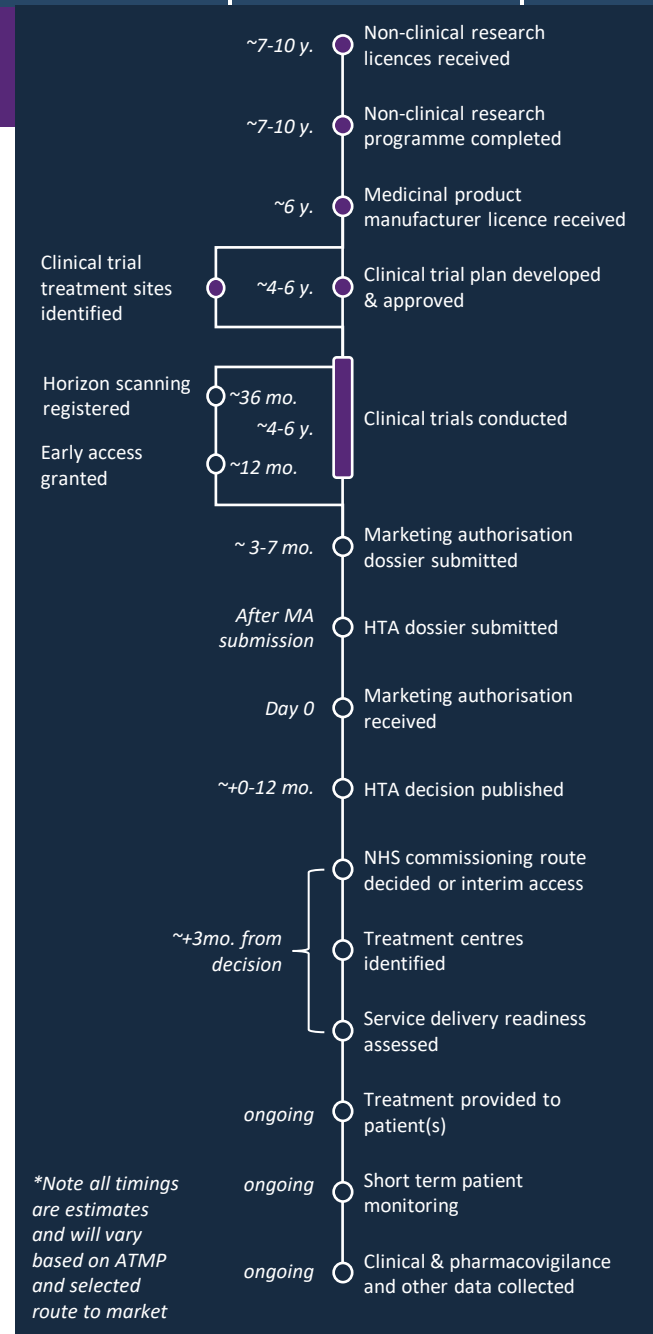
ATMP developers should ensure that all record-keeping and reporting requirements are being followed, including:

- Safety and Adverse Event reporting
- Urgent Safety Measures (USM)
- Suspected Unexpected Serious Adverse Reactions (SUSARs)
- Good Clinical Practice (GCP) or Protocol breach reporting
- DSUR (Development Safety Update Report) reporting
- Progress reporting

If any substantial amendments are made to the clinical trial these should be submitted for MHRA approval via IRAS.

The MHRA will also conduct inspections of clinical trials. GCP Inspectors will assess whether organisation sponsoring and/or conducting CTIMPs have systems in place to meet the requirements of the clinical trials regulations. MHRA inspections are risk-based, and therefore subsequent trial phases may not be inspected.

Linked steps | Who is involved? | Best practices & tips



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

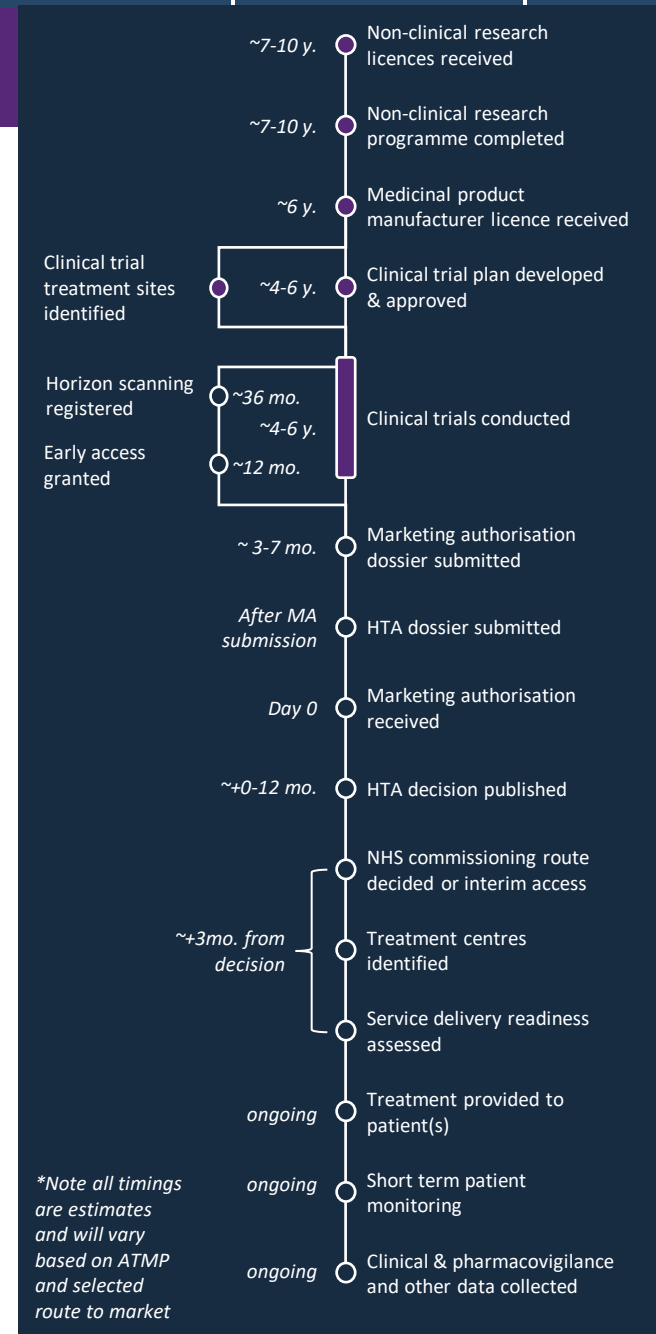
Overview | **To-do list** | Output

- Review full MHRA guidance on safety reporting here
  - Review HRA guidance on safety reporting here
- Inform the MHRA of USMs taken
  - To determine if measure is a USM call MHRA's Clinical Trials Unit on 020 3080 6456
  - Written notification of USMs must be sent to clintrialhelpline@mhra.gov.uk
- Report SUSARS to the MHRA here
- Review MHRA guidance on GCP & serious breach reporting here
  - Serious breaches must also be reported to the relevant ethics committee at the same time as the MHRA
- Review guidance from the MHRA on DSURs here
  - Details on what to include in a DSUR can be found here
  - Submit DSURs to the MHRA through the MHRA submissions portal
- Review NHS guidance on preparing for MHRA Inspection here
- Substantial amendments must be submitted for MHRA approval via the IRAS amendment tool here

**When**

- Fatal or life-threatening SUSARs as soon as possible, but no later than 7 days after you are first aware of the reaction and any other relevant information within 8 days of the report
- DSURs must be submitted every reporting period

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

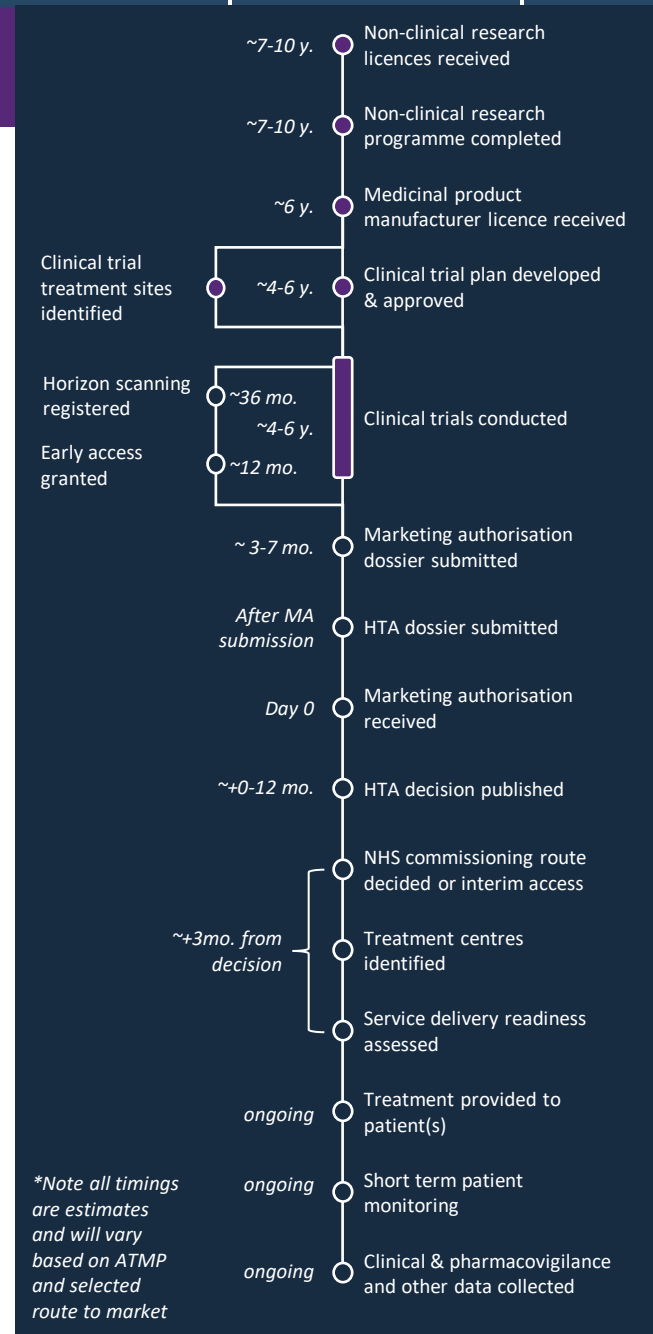
## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

Overview | To-do list | **Output**

- Clinical trial reports

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

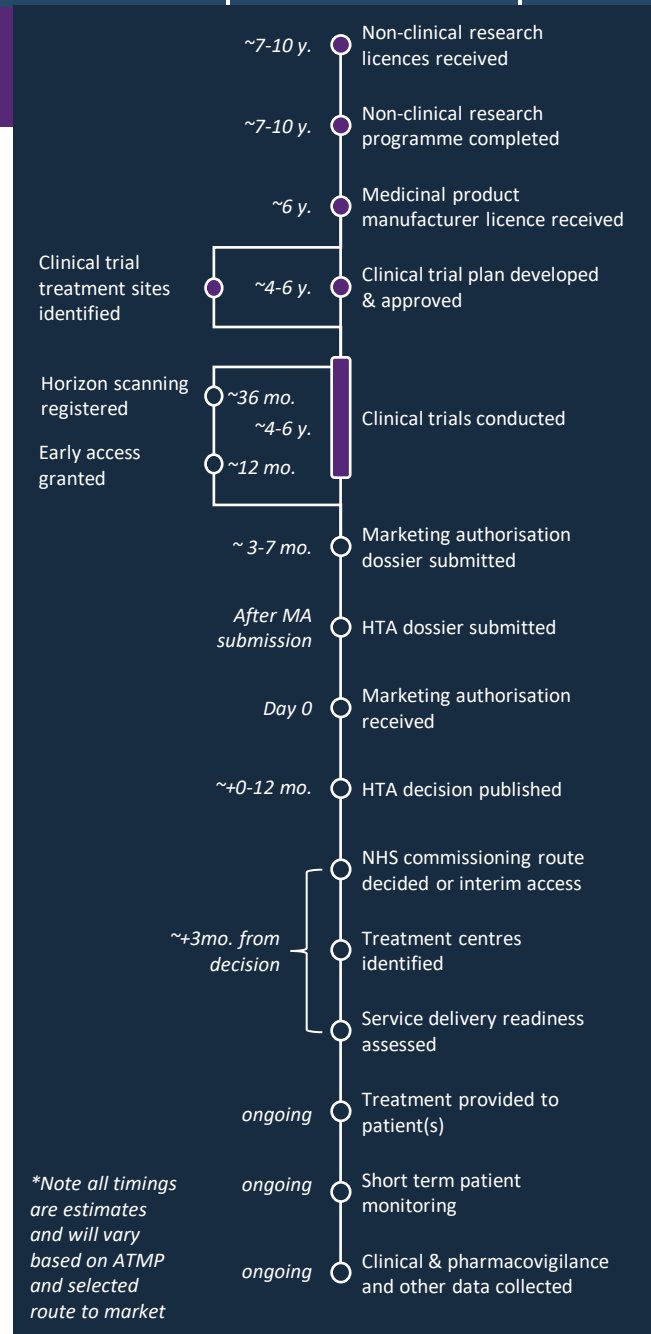
## Overview

## To-do list

## Output

Research documentation consolidation

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

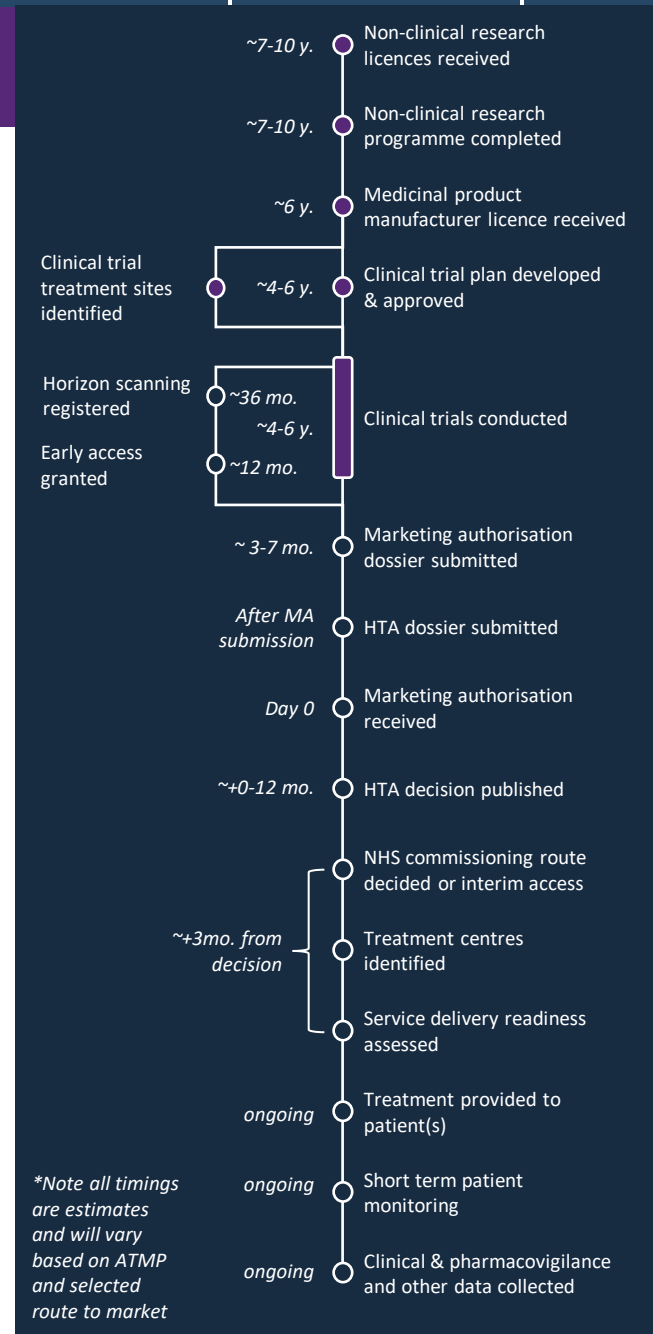
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- HRA

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- **Clinical trial reporting**
- End of trial declaration
- Subsequent trial phase completion
- Horizon scanning registration

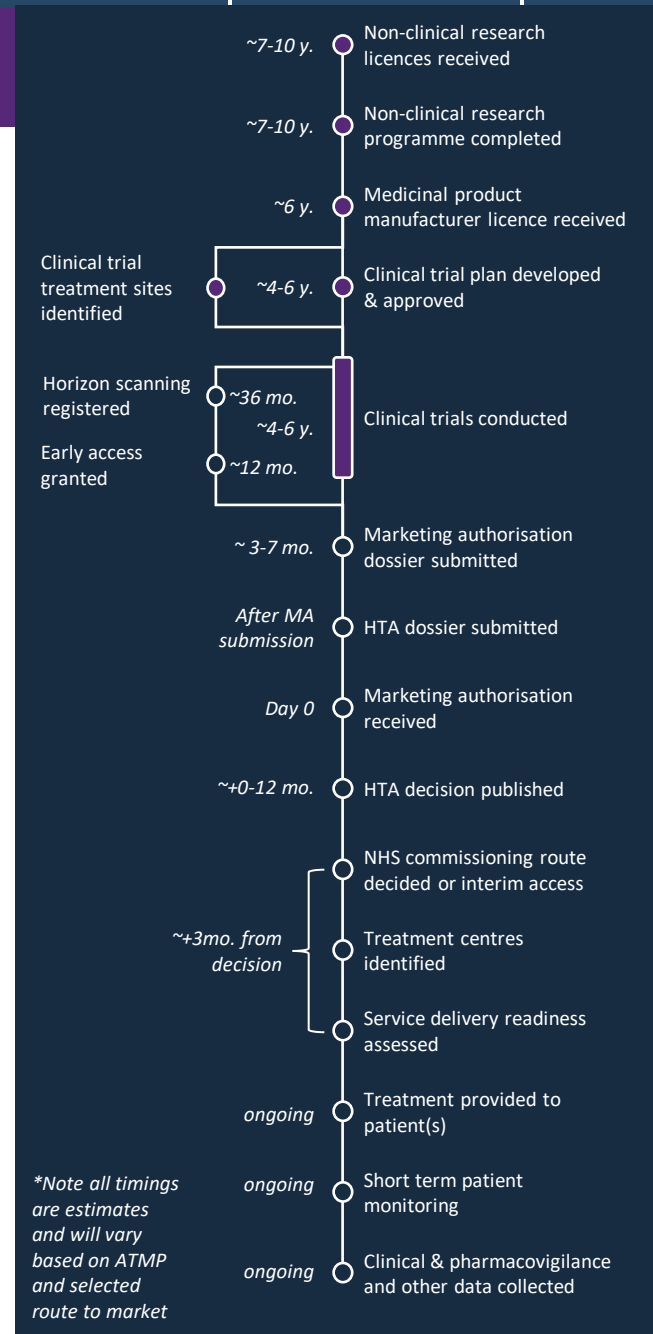
## Overview

## To-do list

## Output

- Audits on the clinical trial documentation may also be carried out

**Linked steps** **Who is involved?** **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

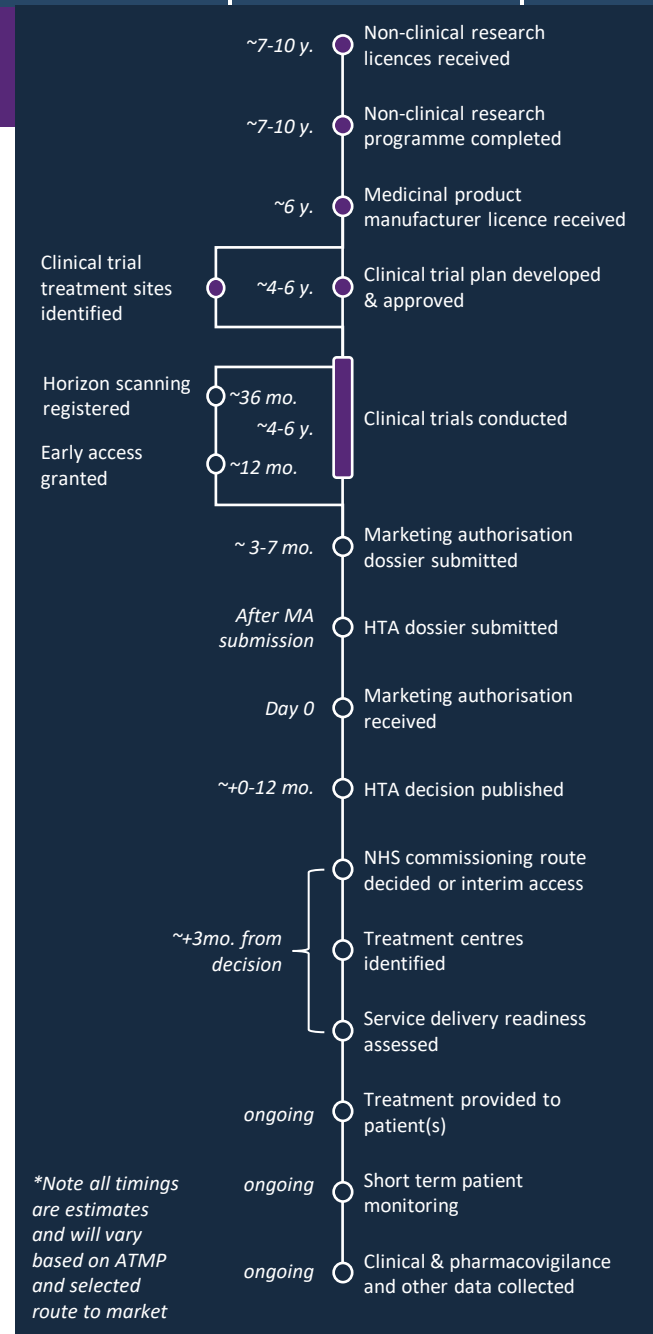
**Overview** | To-do list | Output

Following the end of a trial, the declaration of the end of a trial form must be sent to MHRA to the Research Ethics Committee (REC) or Health Research Authority (HRA).

ATMP developers should also ensure compliance with any agreements in place regarding notification e.g. notification of hospitals, NHS R&D offices and other relevant stakeholders where this has been agreed or may be beneficial.

Summary analysis and results of the clinical trial must then be uploaded to the clinical trial register (and all public registers where the trial has been registered).

**Linked steps** | **Who is involved?** | **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

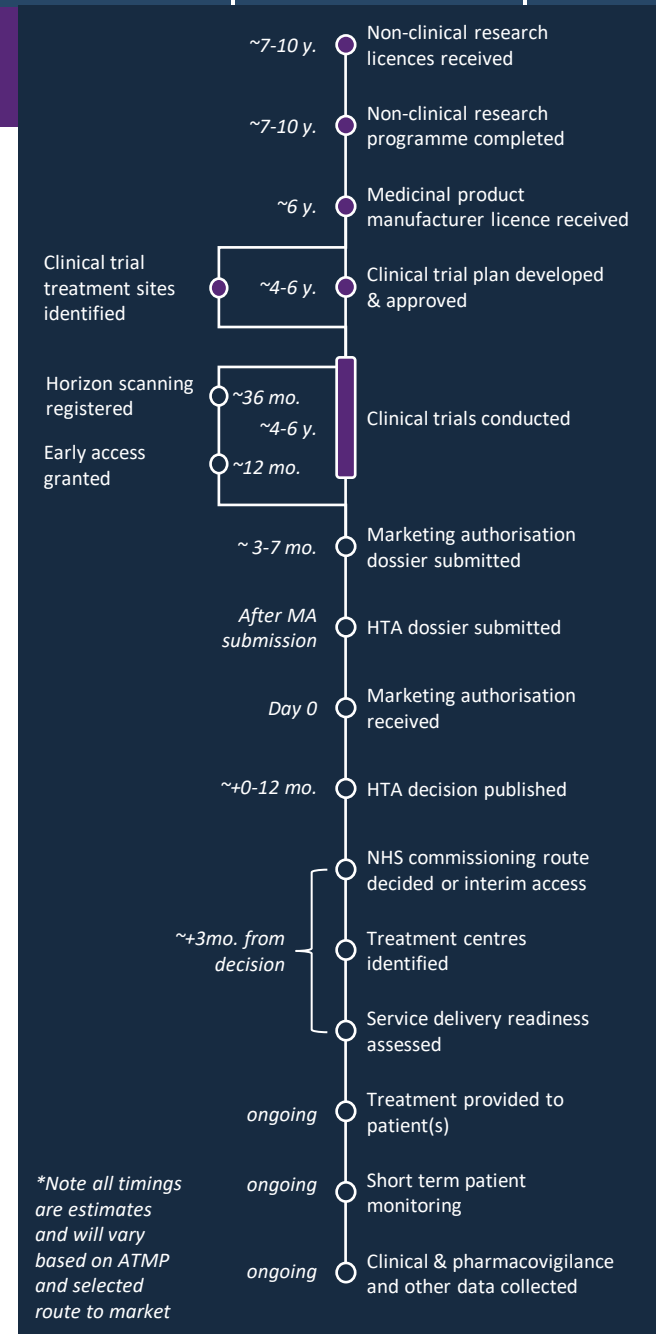
Overview | **To-do list** | Output

- Notify the MHRA using the end of trial form, guidance can be found here
- Notify the HRA or REC using the end of trial form, guidance can be found here
- Upload results of the clinical trial study to the publicly accessible clinical trial register (or registers) where the clinical trial was initially registered

### When

- End of trial form submitted within 90 days of trial end
- If a clinical trial ends prematurely, the form must be submitted within 15 days of trial end
- Summary report submission within 1 year of end of trial (or within 6 months for paediatric studies)

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1** What steps are required for clinical trial application?

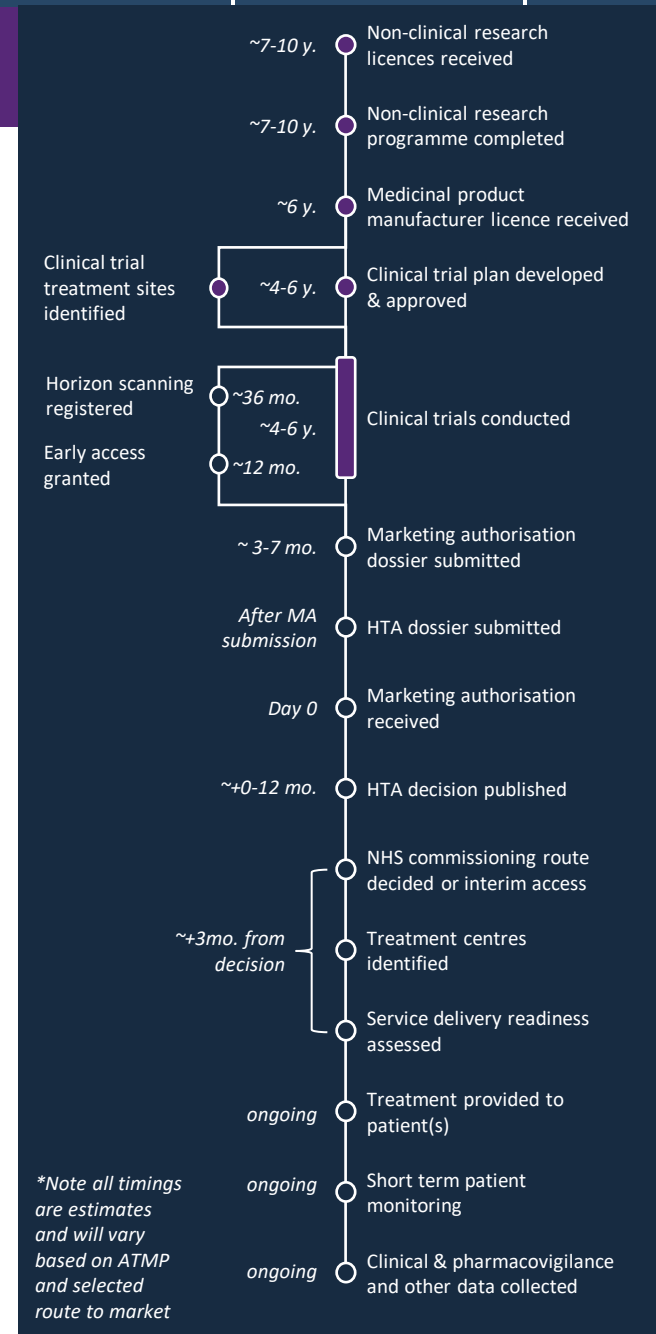
**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

Overview | To-do list | **Output**

- End of clinical trial notification
- Clinical trial results




**Linked steps** | **Who is involved?** | **Best practices & tips**

**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

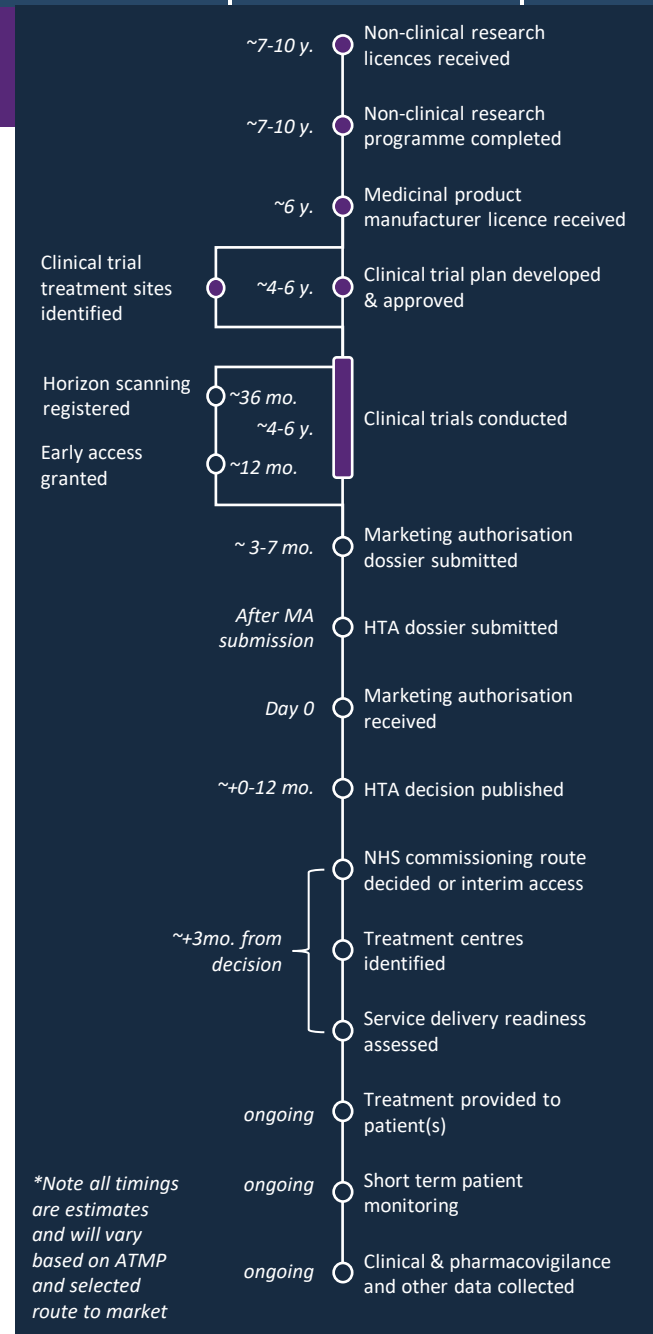
## Overview

## To-do list

## Output

Clinical trial registration

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

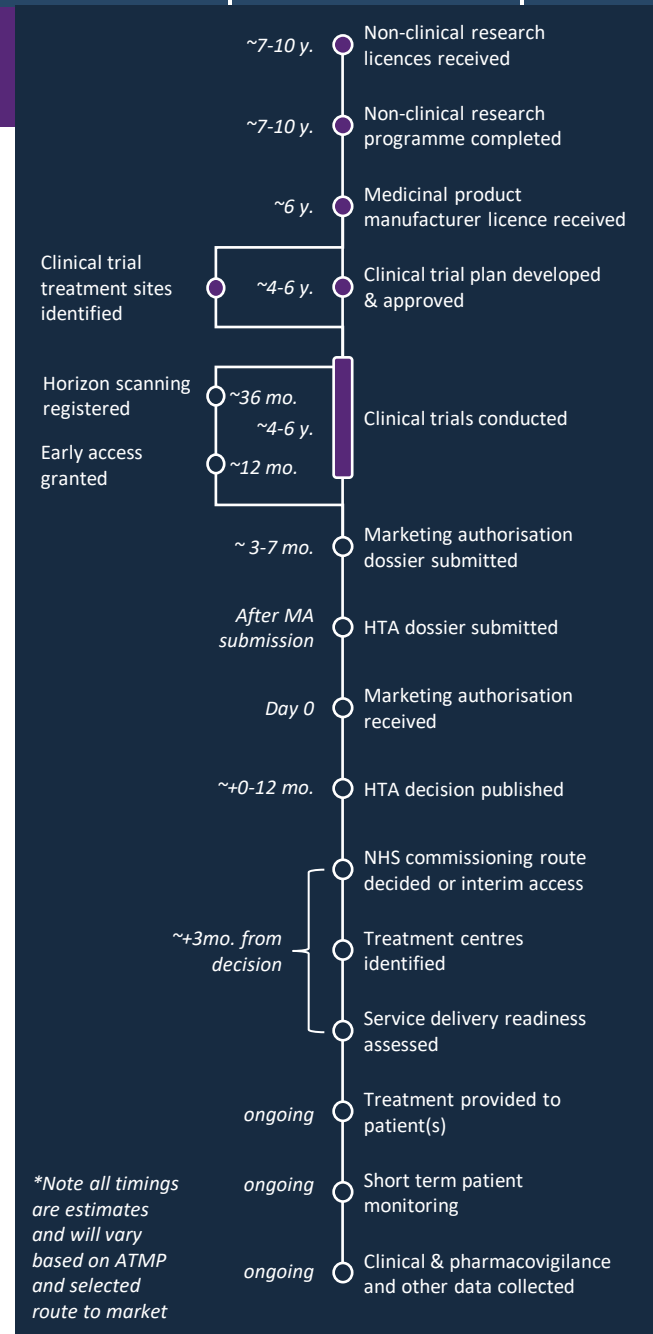
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- HRA

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

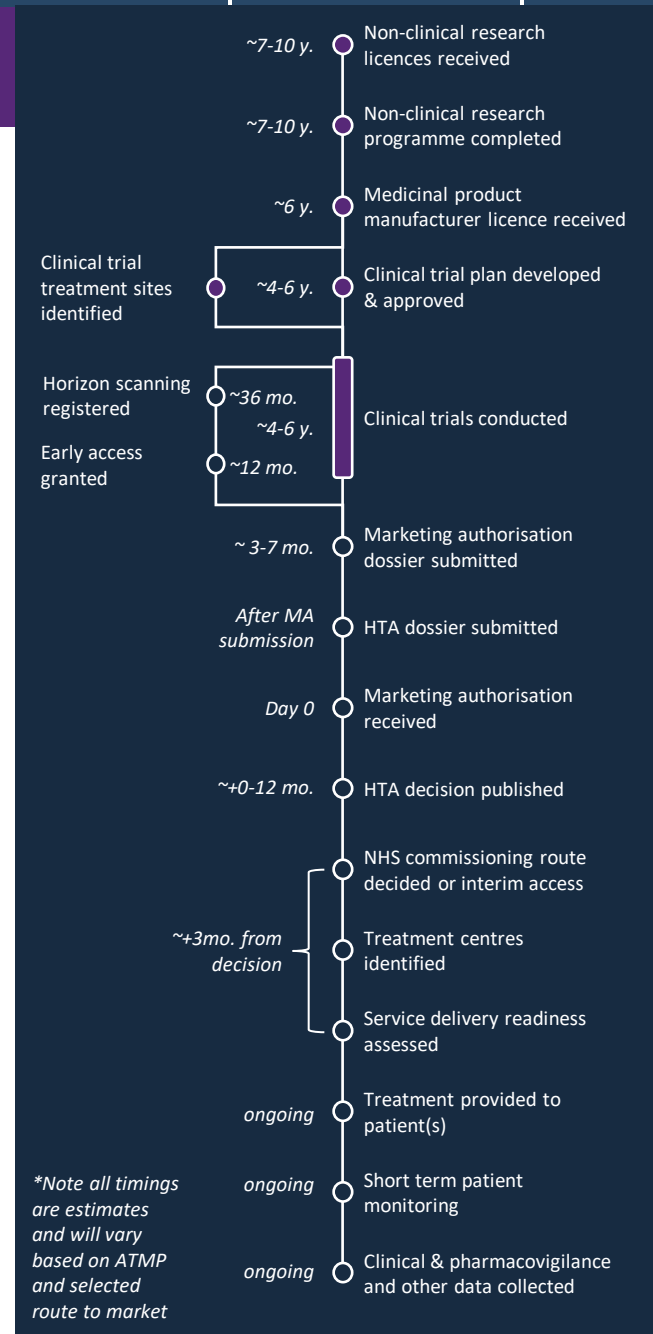
## KEY TOPICS

- Clinical trial reporting
- **End of trial declaration**
- Subsequent trial phase completion
- Horizon scanning registration

Overview | To-do list | Output

- Support for statistical analysis of results is available from a variety of sources such as the UKCRC Clinical Trials Unit, EMA guidance on statistical principles for clinical trials, or CONSORT. However, use of a professional statistician is recommended.

**Linked steps** | **Who is involved?** | **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

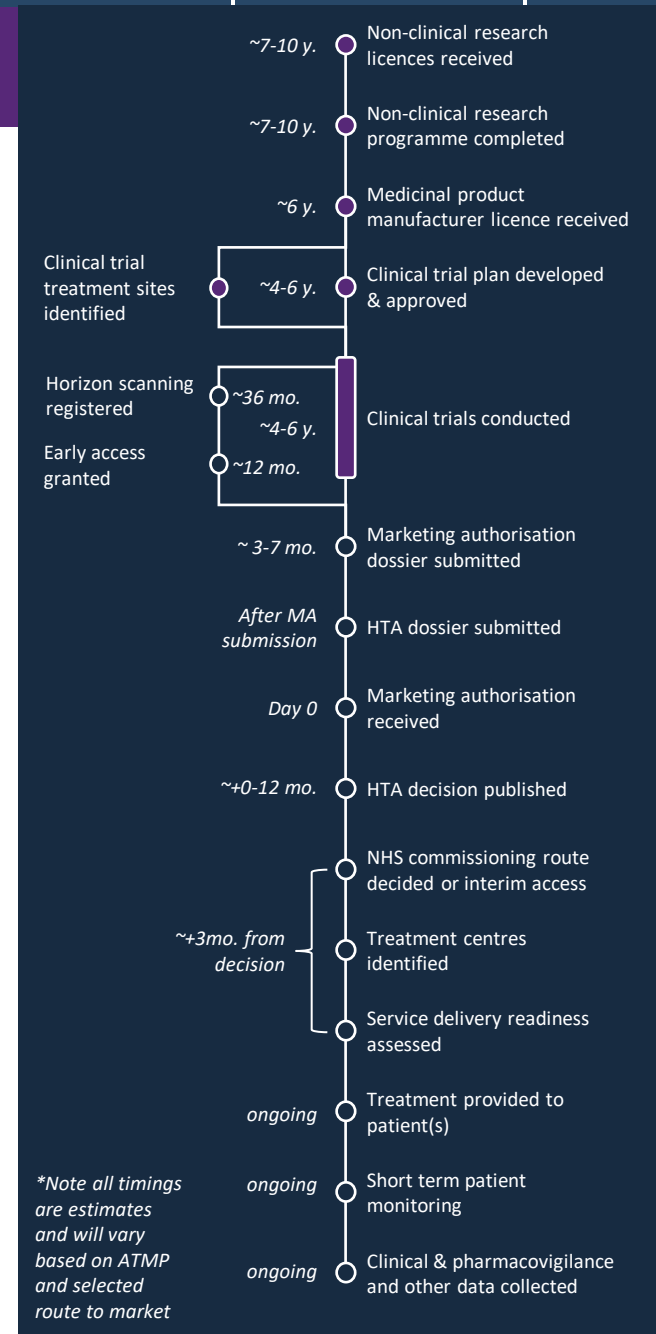
- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

**Overview** | To-do list | Output

All of the previous steps and permissions/approvals are required regardless of the trial phase.

ATMP developers should ensure that any updates to their manufacturing process, quality control processes, formulations, or any other changes are considered and documented before starting subsequent phases.

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

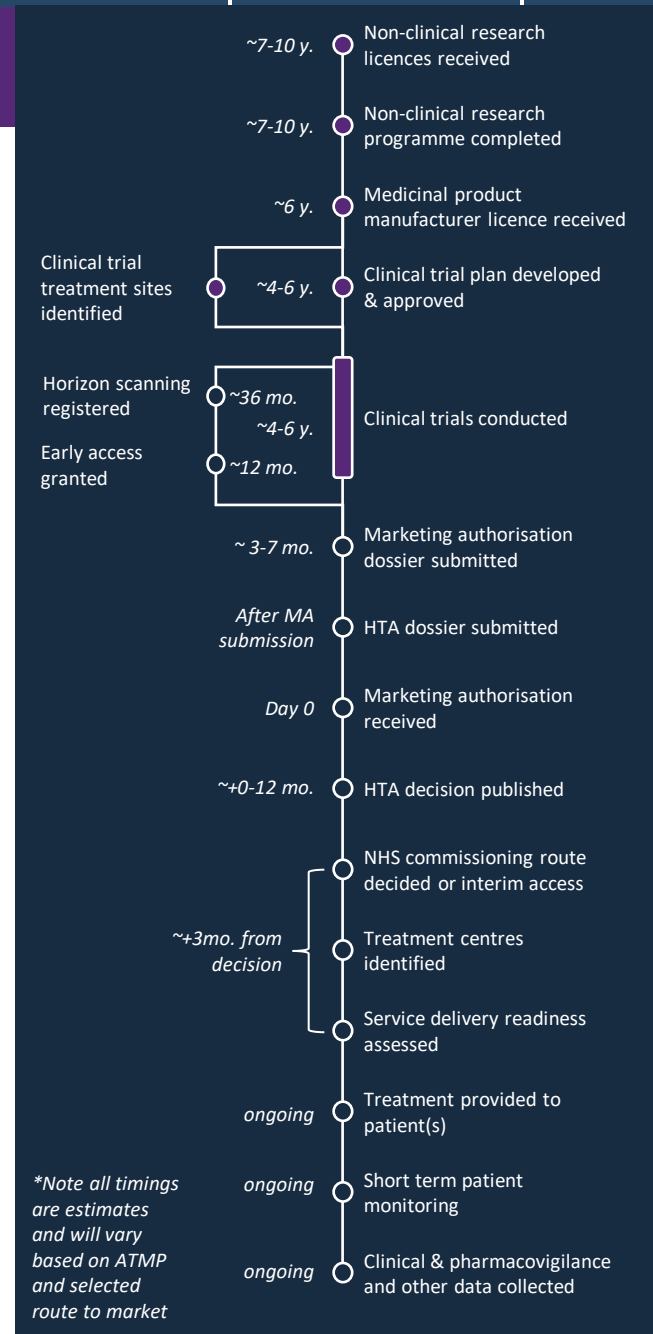
Overview | **To-do list** | Output

- Refer to previous topics for clinical trials
- ATMP developers can also register with the NHS Innovation service here, at any point throughout the development process

### When

After completion of each successful trial phase (and until sufficient evidence generated for Marketing Authorisation Application)

**Linked steps** **Who is involved?** **Best practices & tips**



1 What steps are required for clinical trial application?

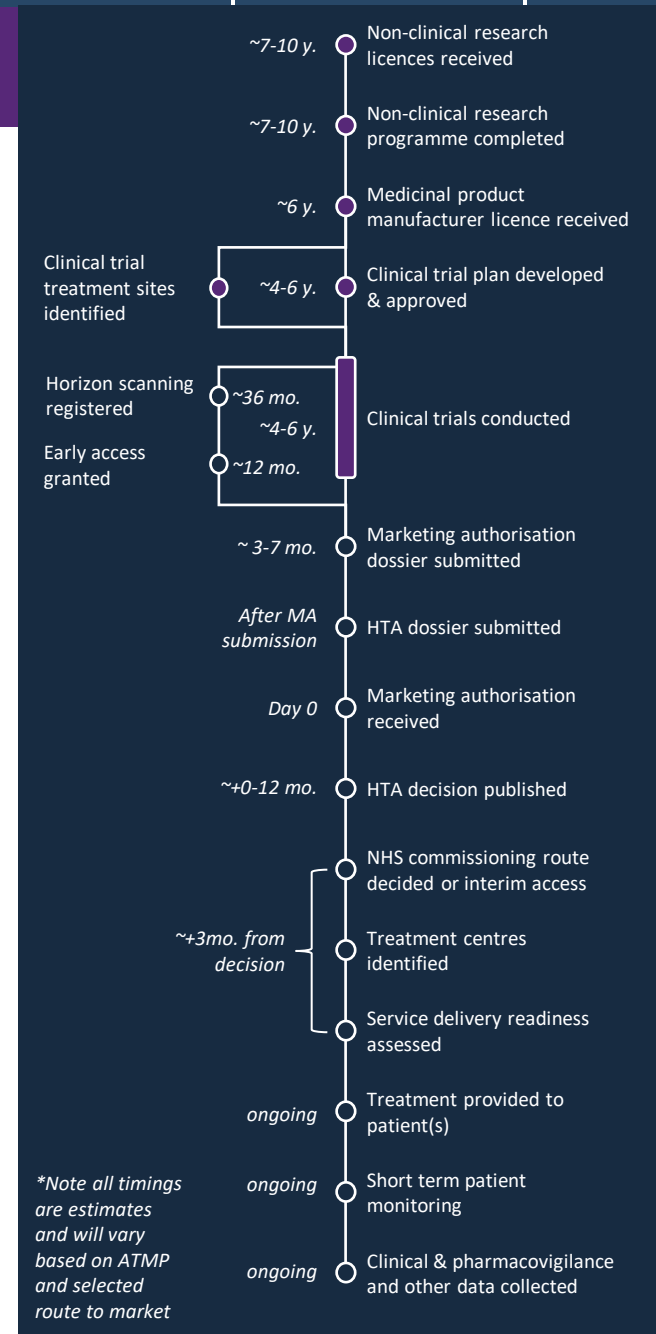
2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

Overview | To-do list | **Output**

- Subsequent phase trial outputs
- Updated manufacturing processes



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

## Overview

## To-do list

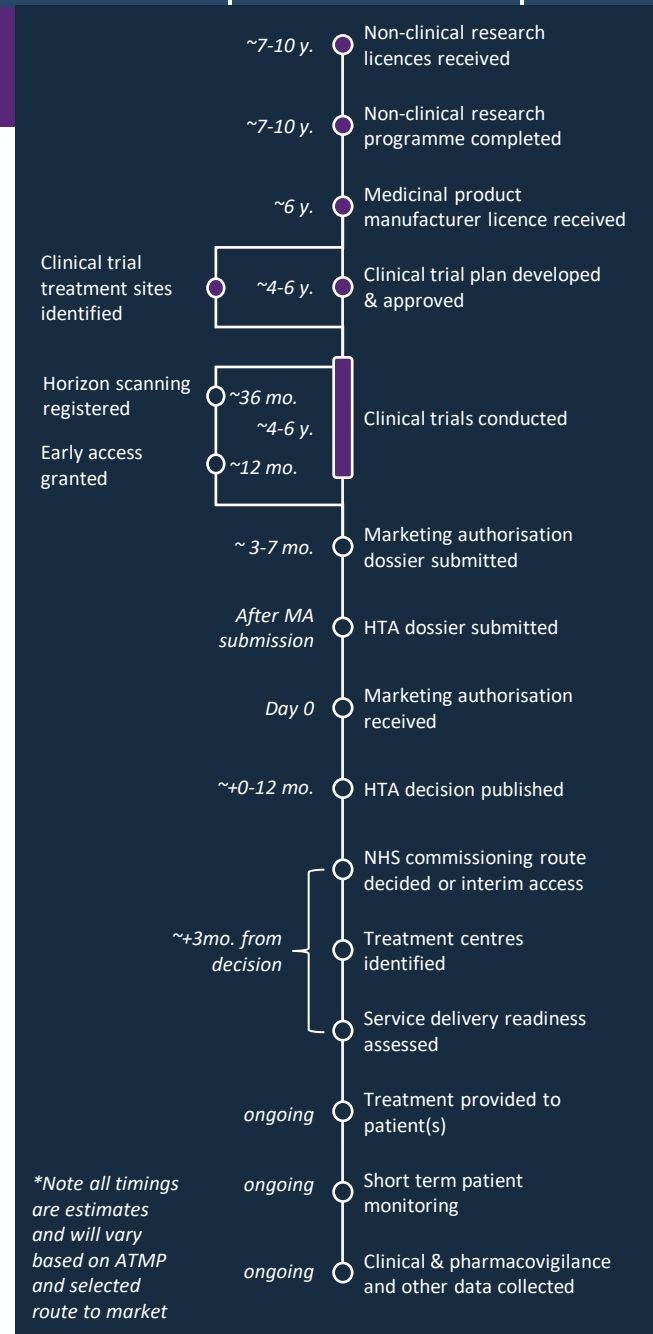
## Output

Clinical trial planning, design and protocol development

Clinical Trial Authorisation

Manufacturing and supply chain planning

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

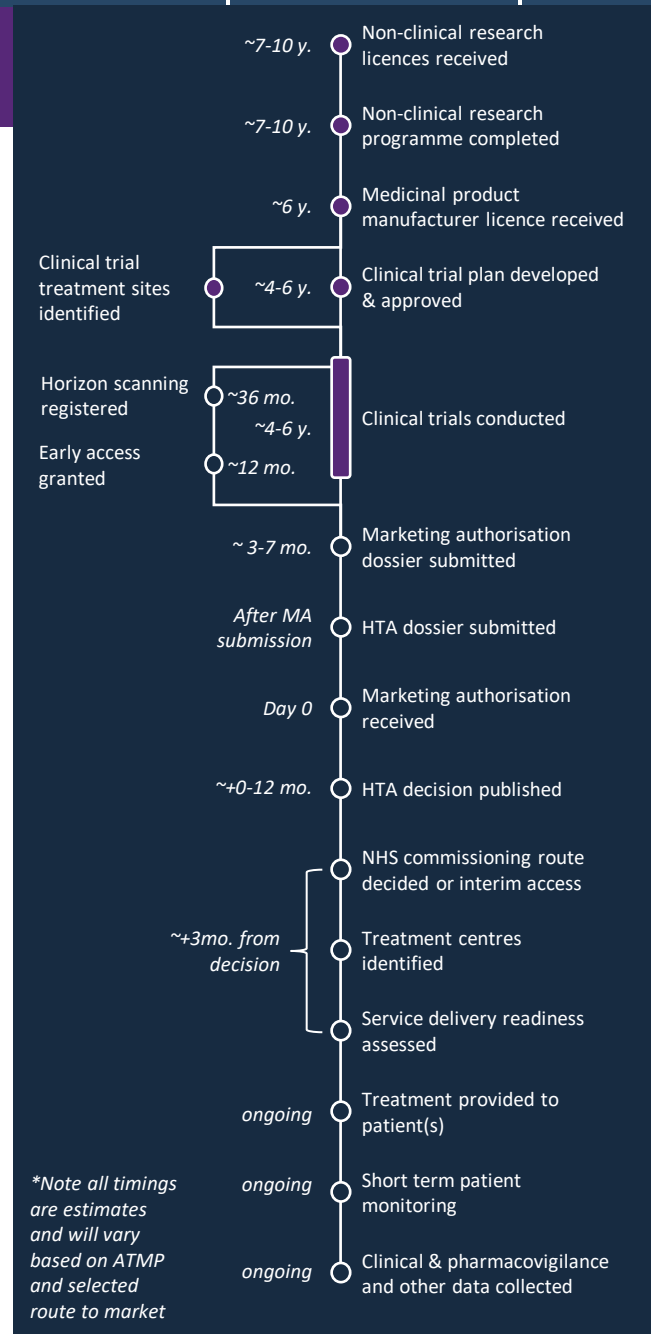
## Overview

## To-do list

## Output

- ATMP developer

**Linked steps** | **Who is involved?** | **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- **Subsequent trial phase completion**
- Horizon scanning registration

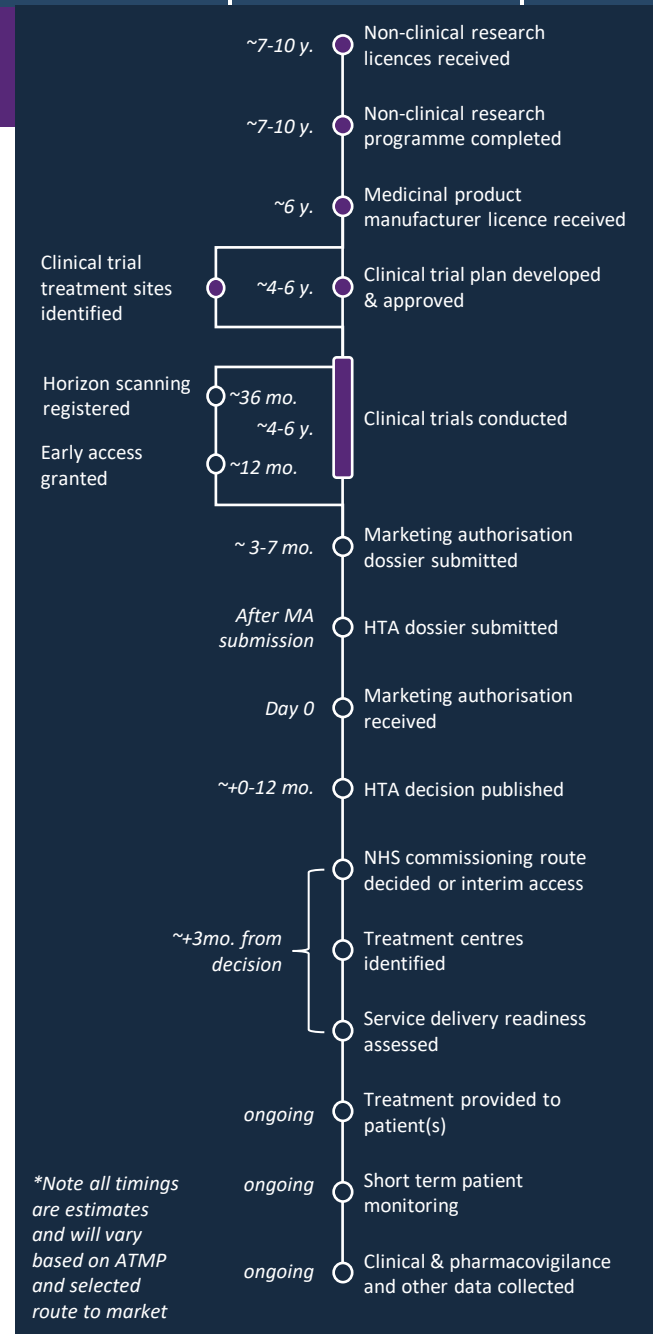
## Overview

## To-do list

## Output

- For later stage trials, payer assessment input from NICE and/or OMA is highly recommended to include and shape clinical trial planning and design
- ATMP developers should conduct confirmatory clinical trials with a product based on a mature manufacturing process, specifications should match those for marketing authorisation as closely as possible as deviations from this principle will lead to comparability issues, a particular challenge for ATMPs

**Linked steps** **Who is involved?** **Best practices & tips**



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS



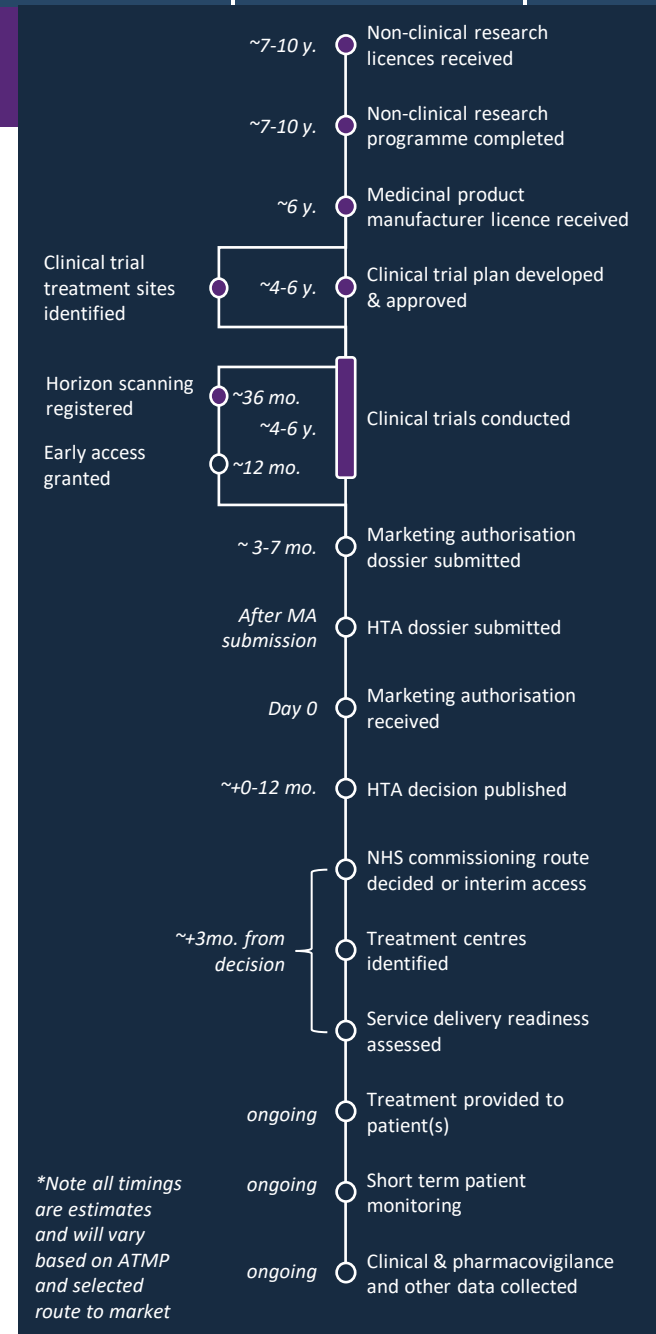
**Overview** | To-do list | Output

ATMP developers should register with UK Pharmascan and enter data regarding their ATMP, indications and formulations in the pipeline. This allows Horizon Scanning organisations and other stakeholders (such as NHS Specialist Pharmacy Service, NICE, NIHR's Innovation Observatory in England and SMC in Scotland and AWTTC in Wales) to gain awareness of ATMPs in development and allow for better preparation of the healthcare system.

The data from PharmaScan is also used for

- Pathway and system planning
- Development of health technology appraisal (HTA) schedules
- Production of briefings and resources for the NHS in England, Scotland and Wales

Linked steps | Who is involved? | Best practices & tips



1 What steps are required for clinical trial application?

2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- Subsequent trial phase completion
- **Horizon scanning registration**

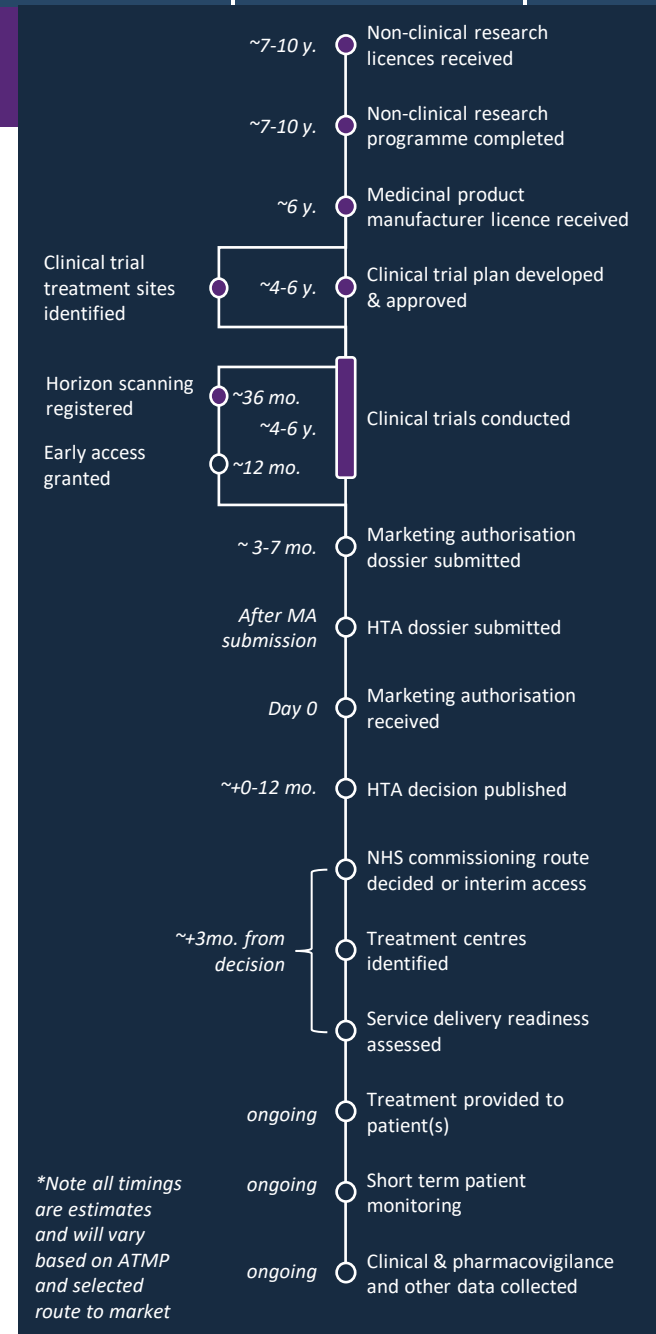
Overview | **To-do list** | Output

- Register to use Pharmascan here
- Once registered, enter product information
  - Further information on using Pharmascan and how to enter data can be found here
- As additional data become available, developers should update their PharmaScan data entries to ensure that information on the ATMP is comprehensive
- Further detail from Pharmascan on how information is used can be found here, and from the ATTC network here
- ATMP developers can also register with the NHS Innovation service here, at any point throughout the development process

**When**

At the start of Phase III trials or 3 years prior to launch, whichever is the earliest

**Linked steps** | **Who is involved?** | **Best practices & tips**



1 What steps are required for clinical trial application?

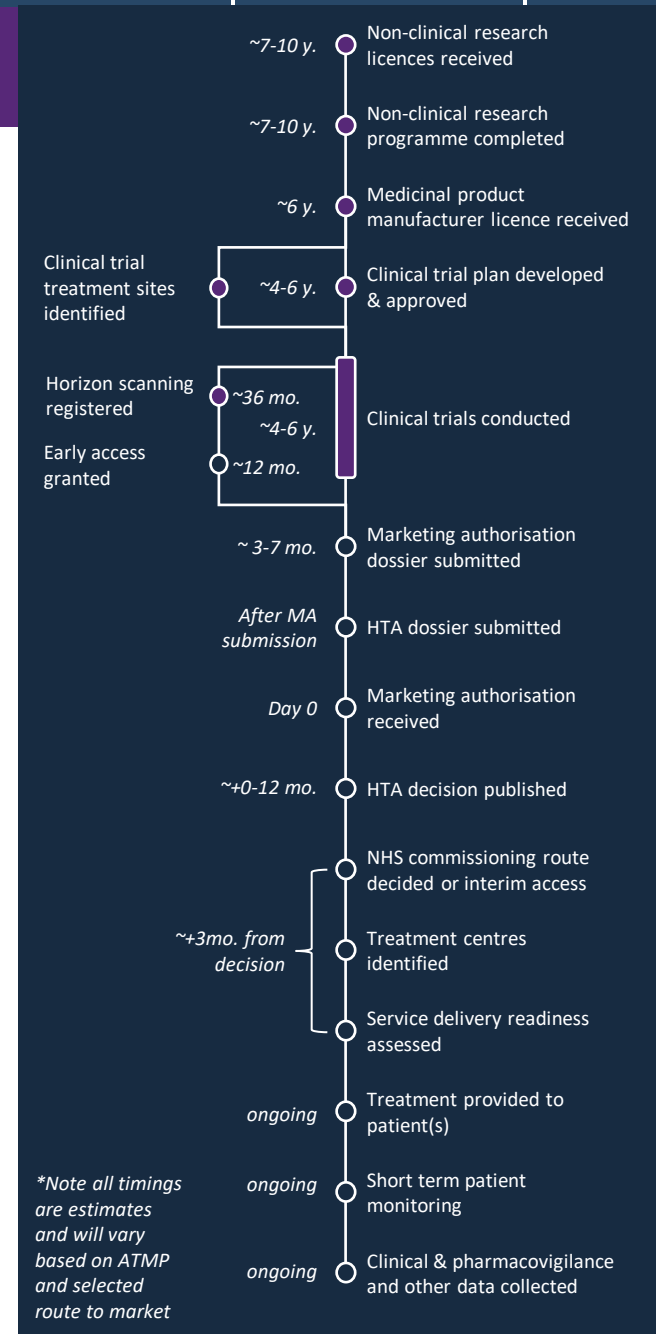
2 What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- Subsequent trial phase completion
- **Horizon scanning registration**

Overview | To-do list | **Output**

- Company registration with Pharmascan
- Data entered into Pharmascan
- Horizon scanning organisations and stakeholders (NICE, NHS England and other national bodies) will use this data for service readiness



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- Subsequent trial phase completion
- **Horizon scanning registration**

## Overview

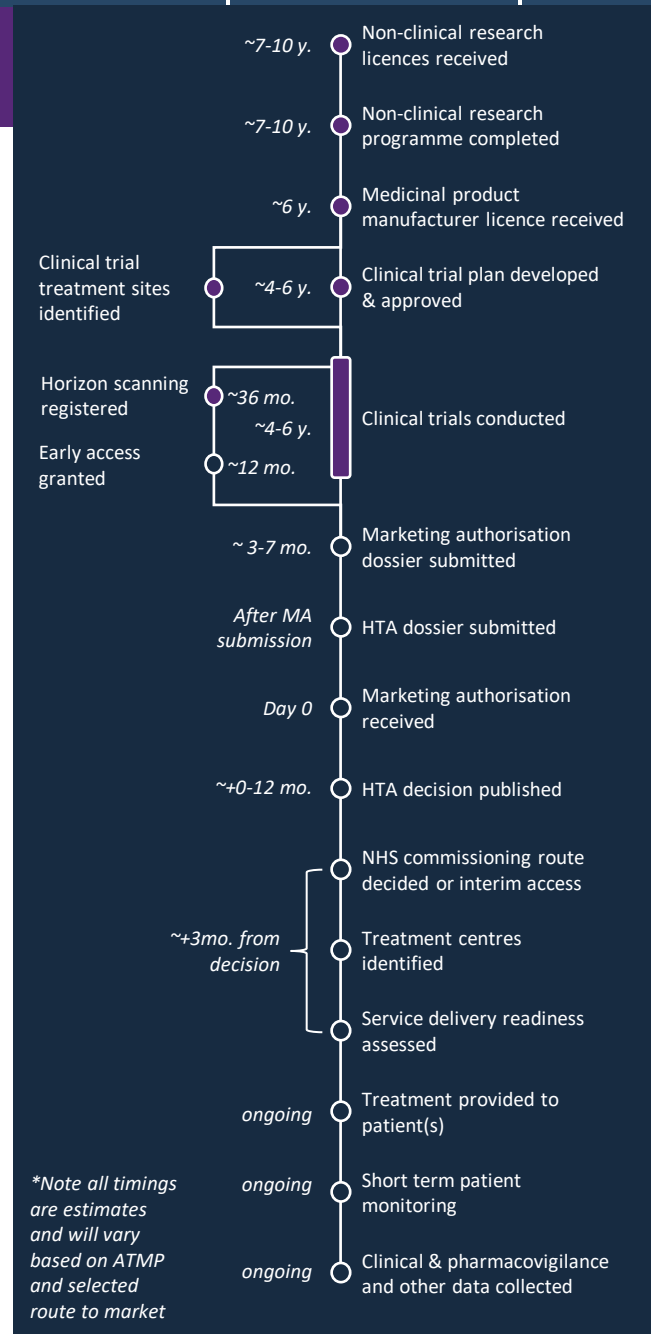
## To-do list

## Output

Health Technology Assessment Technology Appraisal

Health Technology Assessment Highly Specialised Technologies evaluation

**Linked steps** **Who is involved?** **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- Subsequent trial phase completion
- **Horizon scanning registration**

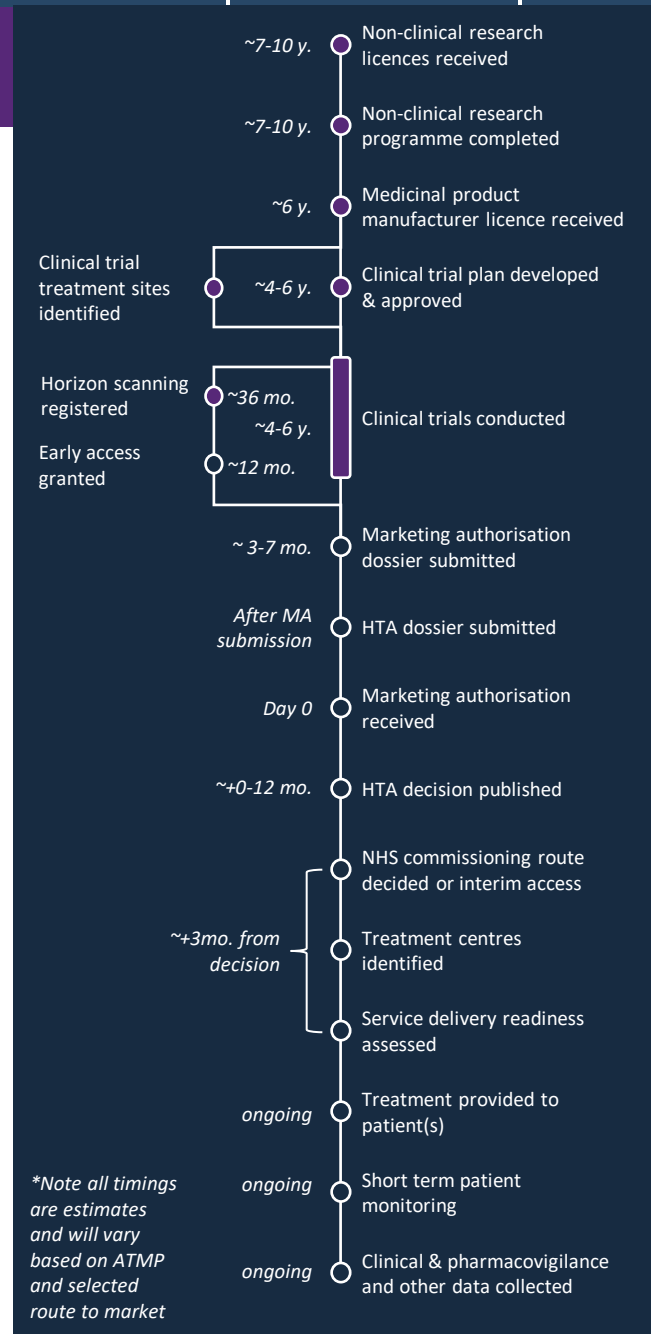
## Overview

## To-do list

## Output

- ATMP developer
- UK Pharmascan

**Linked steps** | **Who is involved?** | **Best practices & tips**



**1** What steps are required for clinical trial application?

**2** What clinical trial steps should be performed prior to marketing authorisation?

## KEY TOPICS

- Clinical trial reporting
- End of trial declaration
- Subsequent trial phase completion
- **Horizon scanning registration**

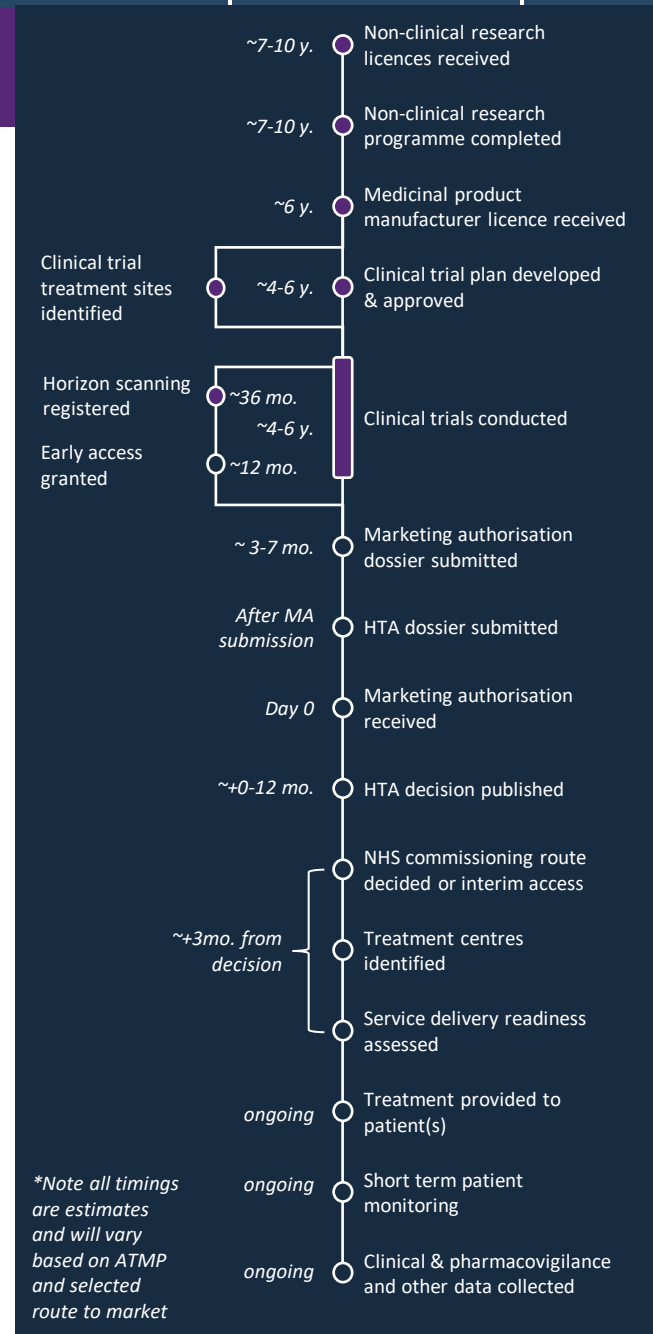
## Overview

## To-do list

## Output

- Developers should be prepared for ongoing engagement with horizon scanning professionals to provide information and clarifications where required

**Linked steps** **Who is involved?** **Best practices & tips**



1 What programmes are available to accelerate time to market?
2 How can an ATMP obtain early access through EAMS?
3 What are the routes for ATMP reimbursement assessment?
4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

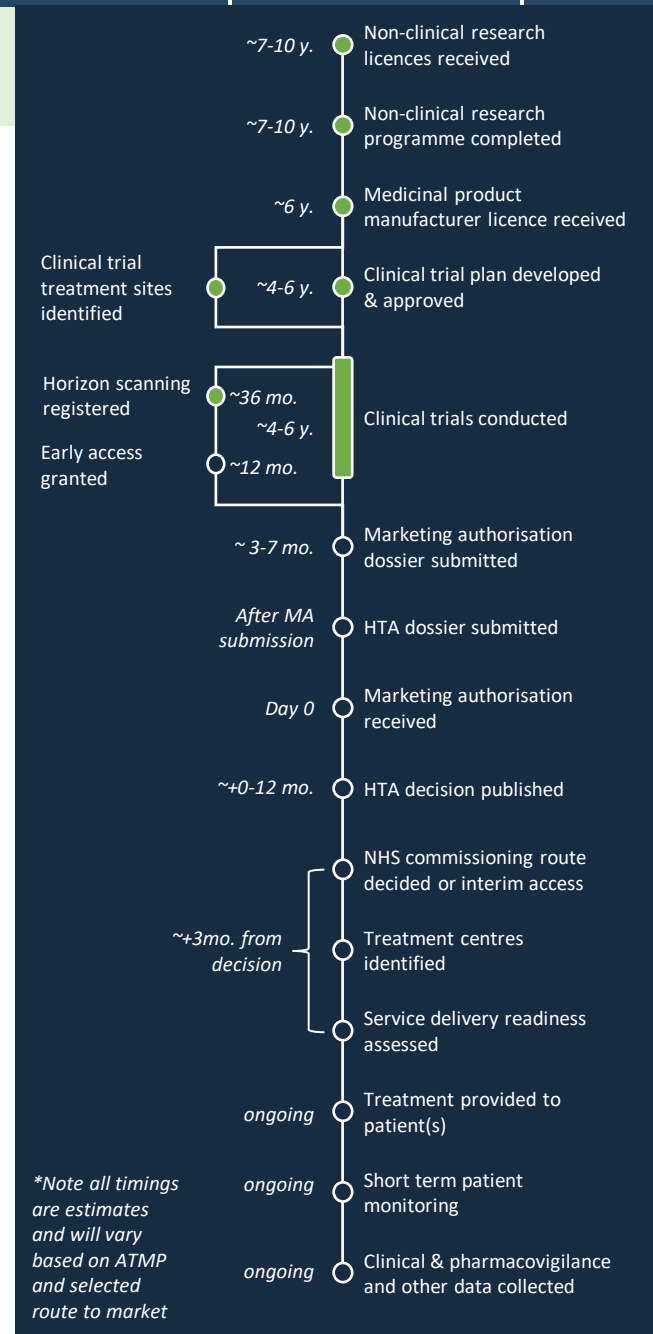
**Overview** | To-do list | Output

The Innovative Licensing and Access Pathway (ILAP) aims to accelerate the time to market, facilitating patient access to medicines. ILAP provides applicants with access to a toolkit to support all stages of the design, development and approvals process, along with opportunities for enhanced regulatory and other stakeholder input.

Developers should review the guidance on ILAP, and, if applicable, apply to the MHRA for Innovation Passport designation. Developers will then be required to attend a meeting with the MHRA regarding their application and receive an outcome decision. There are fees involved for these services.

If successful, Innovation Passport Holders are eligible to receive a customised Target Development Profile roadmap* (TDP) to guide ongoing development, along with early engagement and ongoing advice with the MHRA, NICE and the SMC.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

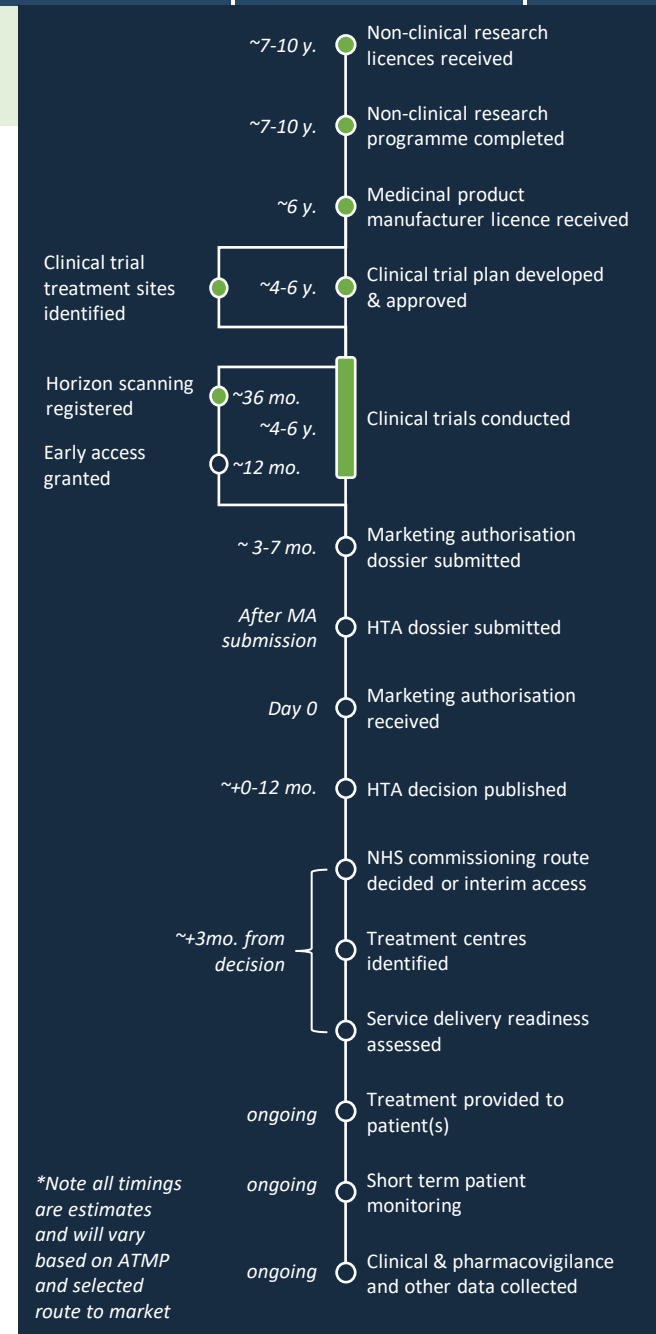
Overview | **To-do list** | Output

- Review the MHRA guidance on the ILAP process here
- Complete the MHRA Innovation Passport application form here
- Meet with the MHRA to discuss how the ATMP meets the application criteria (within 4-6 weeks of the application submission) viewed here
- Receive innovation passport outcome (within 4 weeks of the meeting)
- Submit Target Development Profile (TDP) submission form to the MHRA here
- Review the TDP toolkit here
- Hold TDP meeting with all ILAP partners following positive Innovation Passport outcome

**When**

Developers can apply for ILAP at any point prior to marketing authorisation approval

Linked steps | Who is involved? | Best practices & tips



**1 What programmes are available to accelerate time to market?**

2 How can an ATMP obtain early access through EAMS?

3 What are the routes for ATMP reimbursement assessment?

4 What reimbursement commercial arrangement options are available?

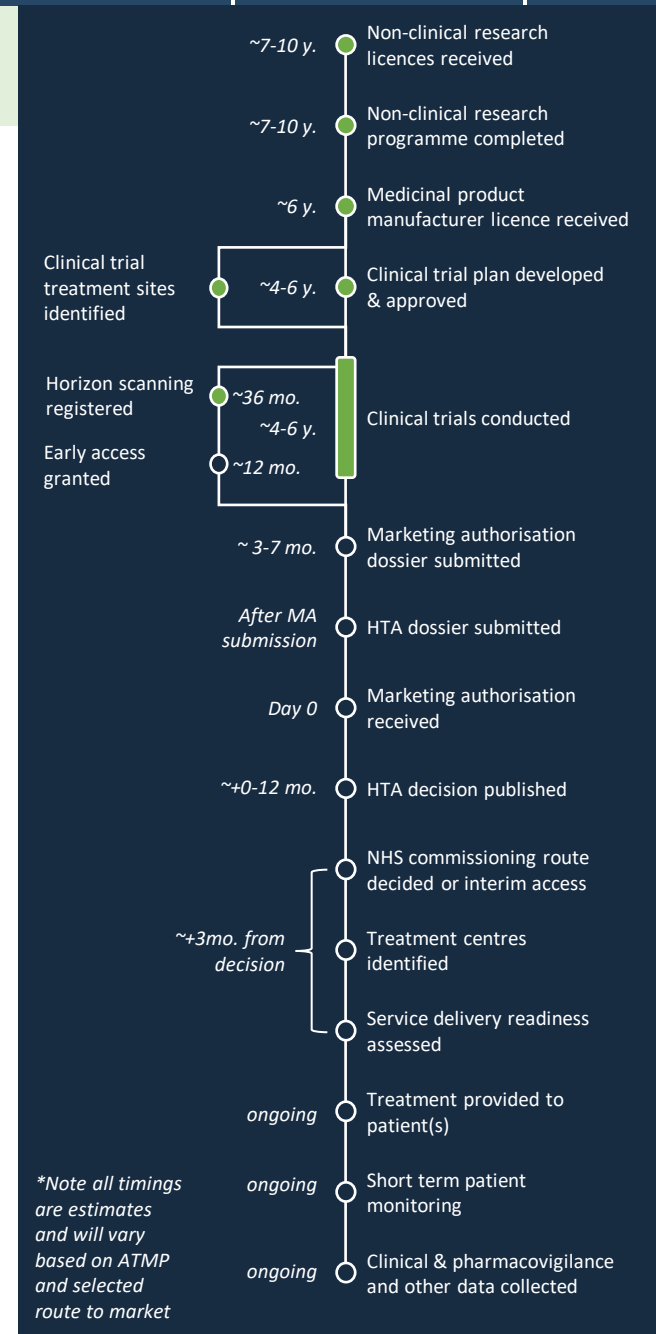
## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

Overview | To-do list | **Output**

- Innovation Passport designation
- Customised Target Development Profile roadmap*
- Ongoing engagement and support from the MHRA, NICE (and SMC and AWTTC as applicable)

*The TDP is available for all developers who are awarded an Innovation passport, however for companies at a later stage of development it may not be relevant




Linked steps | Who is involved? | Best practices & tips

**1 What programmes are available to accelerate time to market?**

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## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

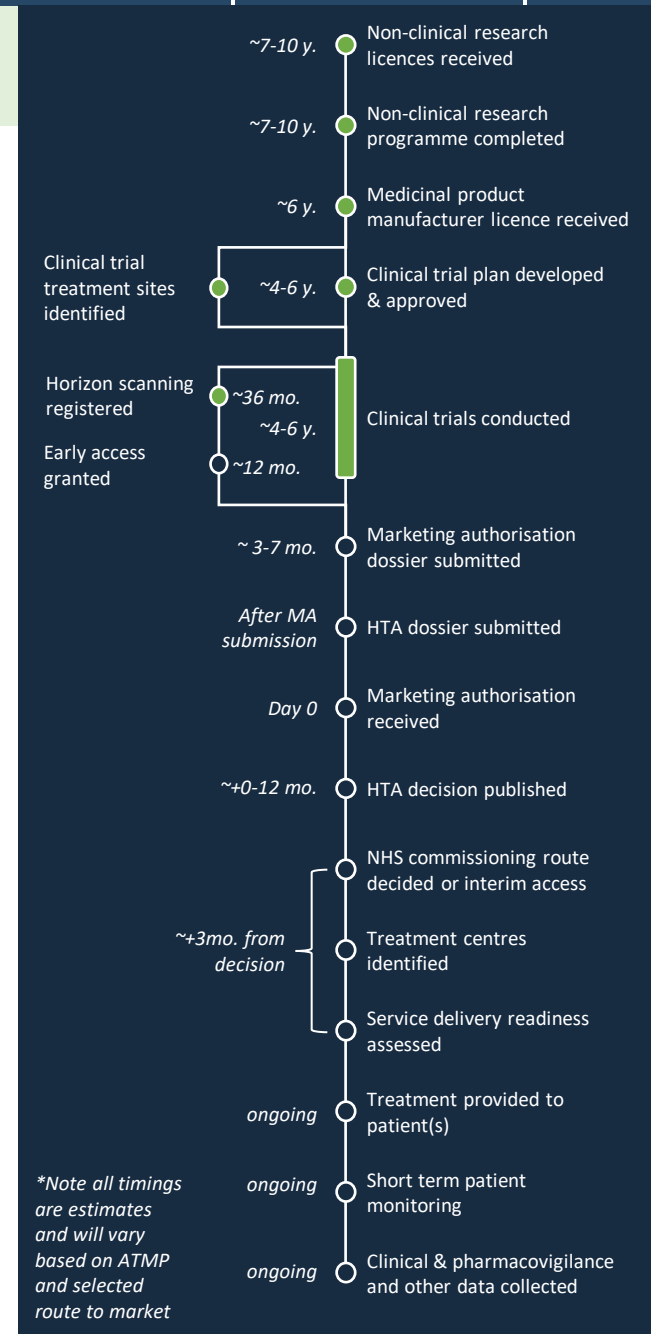
## Overview

## To-do list

## Output

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

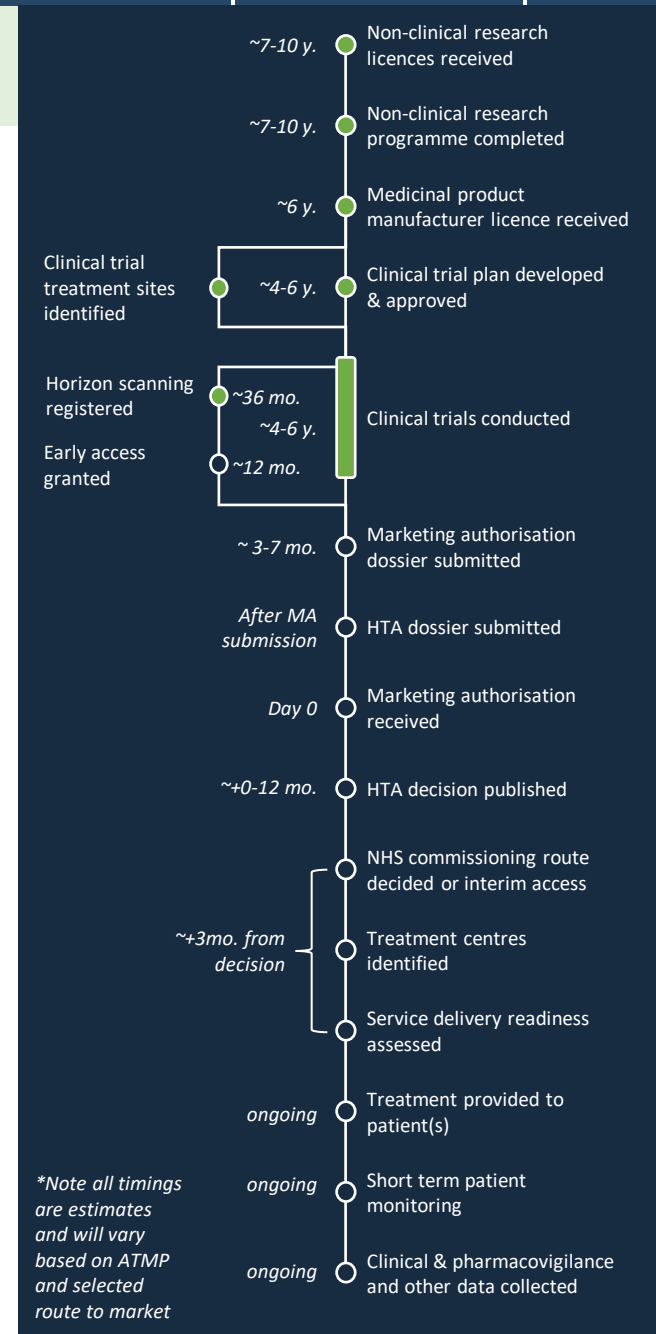
## To-do list

## Output

- ATMP developer

Permanent ILAP partners:
- MHRA
- NICE
- SMC
- AWTTC

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- **Innovative Licensing and Access Pathway (ILAP) [optional]**
- International marketing authorisation coordination via Project Orbis [optional]
- International marketing authorisation coordination via Access Consortium [optional]

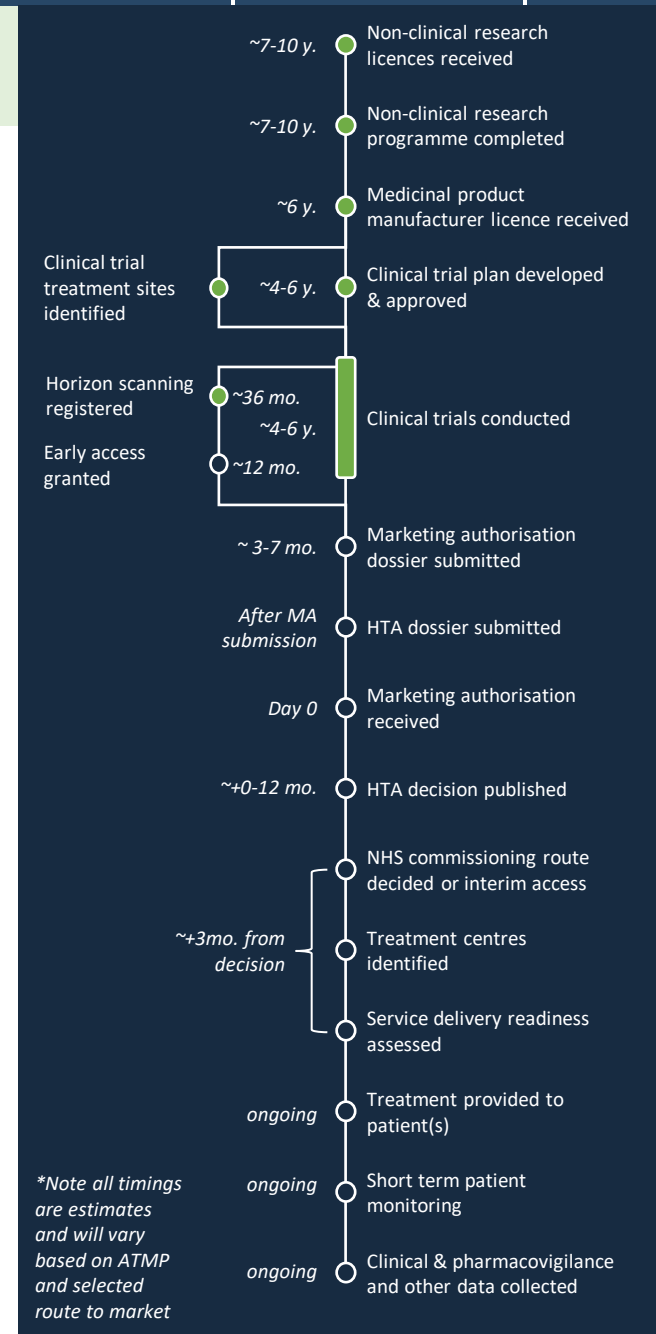
## Overview

## To-do list

## Output

- In order to maximise benefits of ILAP innovation passport, applications should be made early, during non-clinical research phase

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

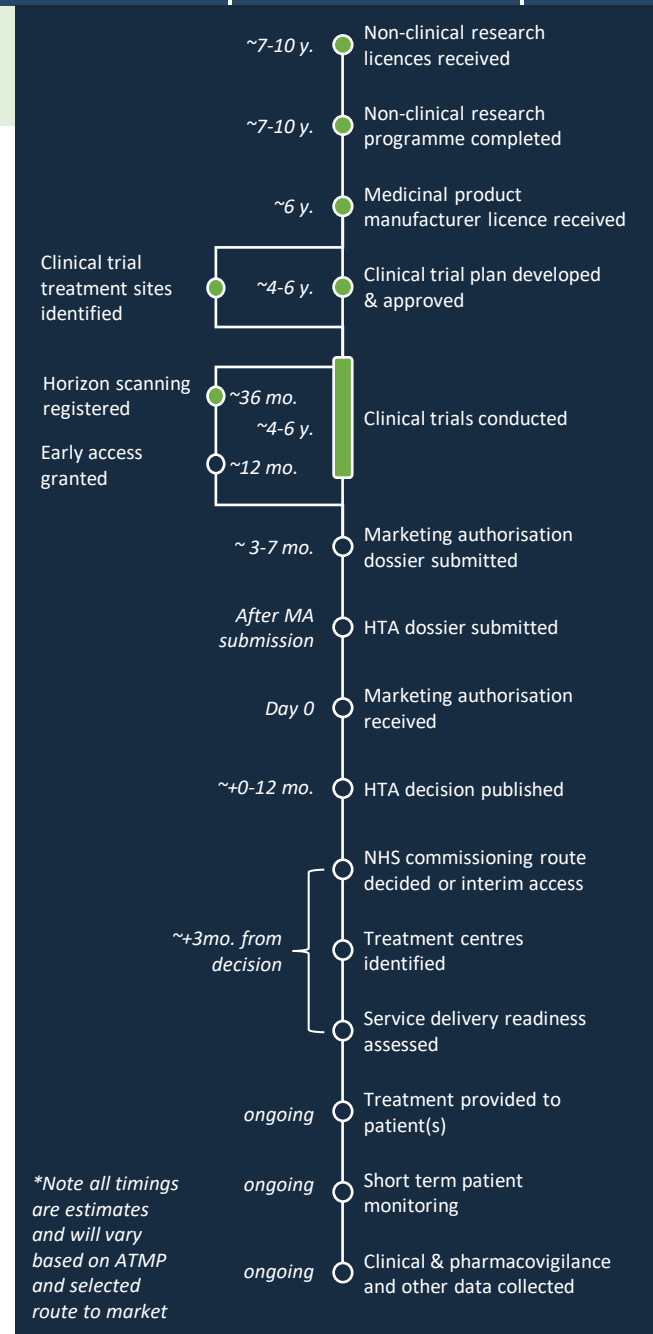


**Overview** | To-do list | Output

Developers of oncology products may submit a request to the MHRA to recommend their product for Project Orbis. Co-ordinated by the FDA, Project Orbis provides a route for concurrent review of marketing authorisation applications for promising cancer medicines from participating countries.

Applicants for Project Orbis are required to have an innovation passport designation, and will still be required to submit their full Marketing Authorisation to the MHRA using their existing process. There are fees involved for these services.





1 What programmes are available to accelerate time to market?
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## KEY TOPICS



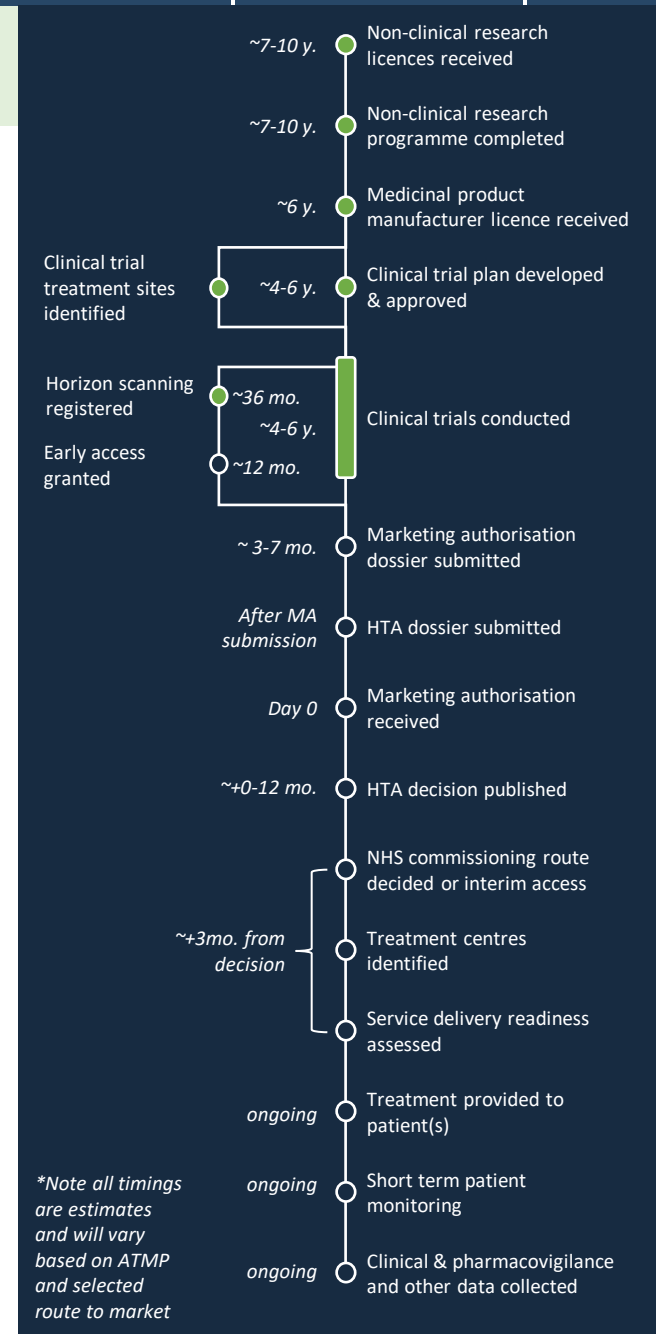
Overview | **To-do list** | Output

- Review Project Orbis guidance here and determine which submission type to use
- If not already completed, submit application through ILAP for Innovation Passport designation here
- Submit request (including a summary of the product and details of eligibility criteria) to the MHRA for them to recommend inclusion in Project Orbis to the FDA via Orbis-MHRA@mhra.gov.uk
- Submit meeting request to MHRA regarding Project Orbis submission via Orbis-MHRA@mhra.gov.uk
- Continue UK submission process along with concurrent submissions with participating countries
- Receive outcome decision from the FDA

### When

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips

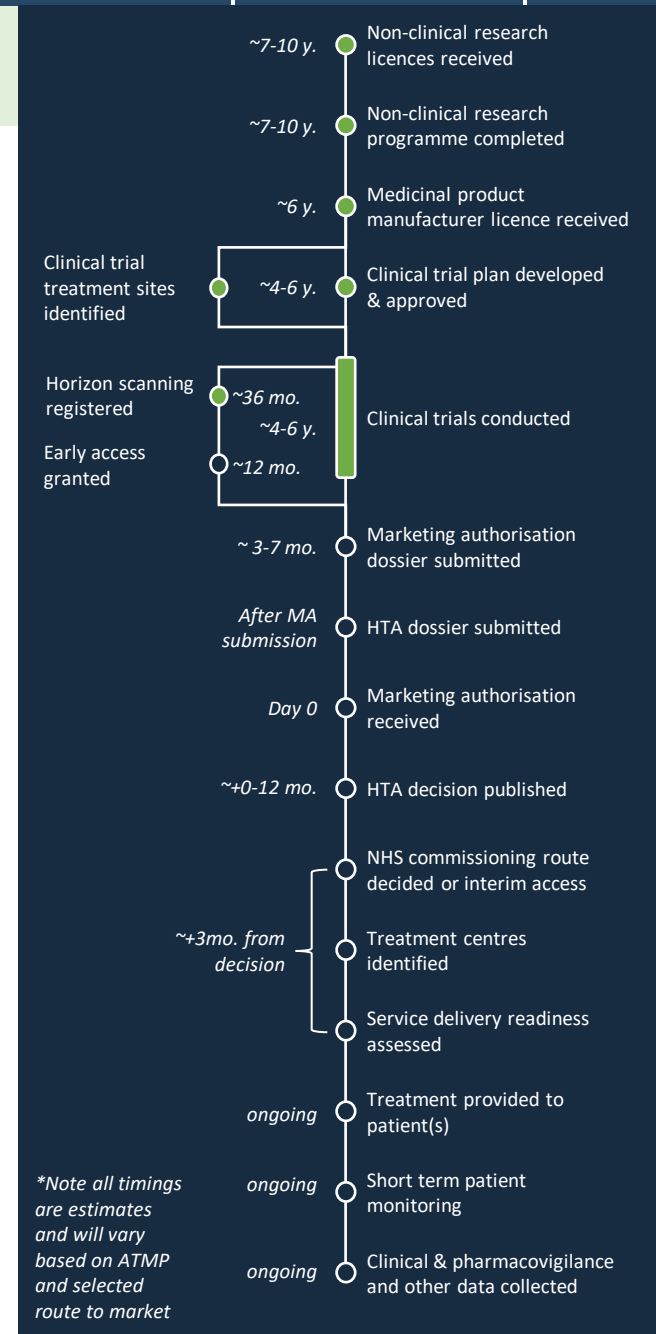


## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

Overview | To-do list | **Output**

- Inclusion or exclusion decision from FDA
- Marketing Authorisation decision from all participating Project Orbis countries



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## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

## To-do list

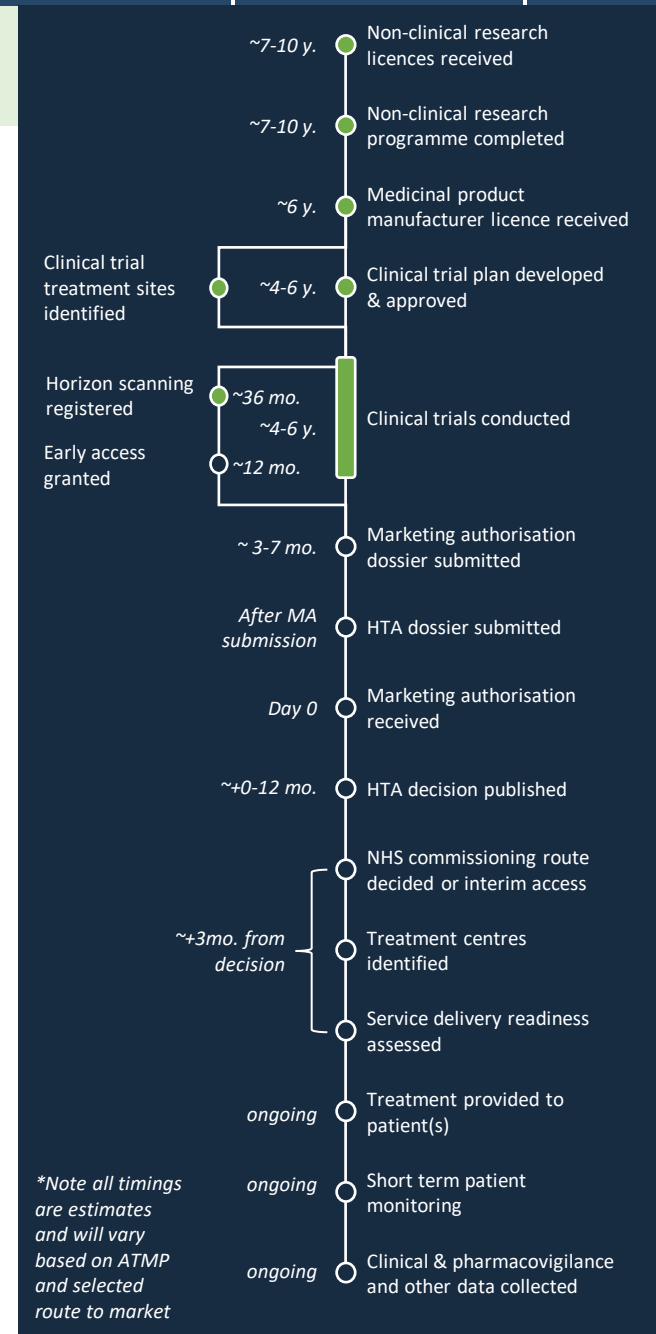
## Output

Marketing Authorisation submission

Innovative Licensing and Access Pathway (ILAP) [optional]

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS



## Overview

- ATMP developer
- MHRA
- FDA

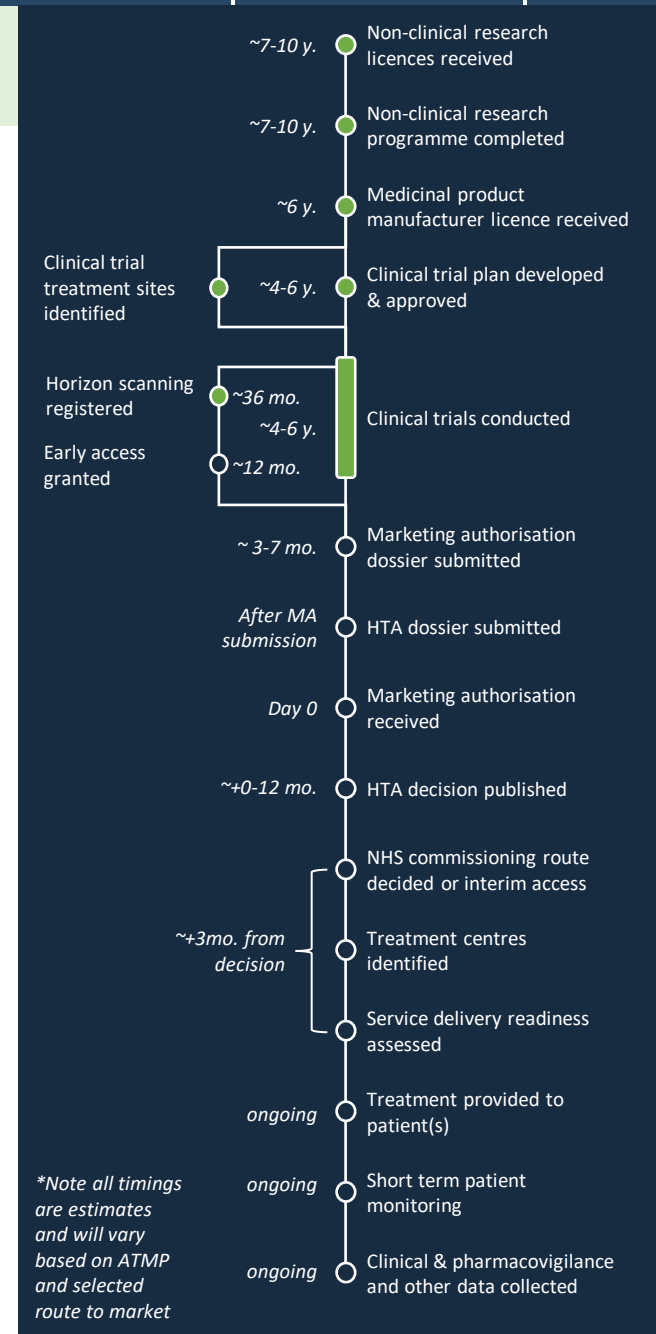
Project Orbis participating countries:

- FDA (USA)
- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)
- ANVISA (Brazil)

## To-do list

## Output

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

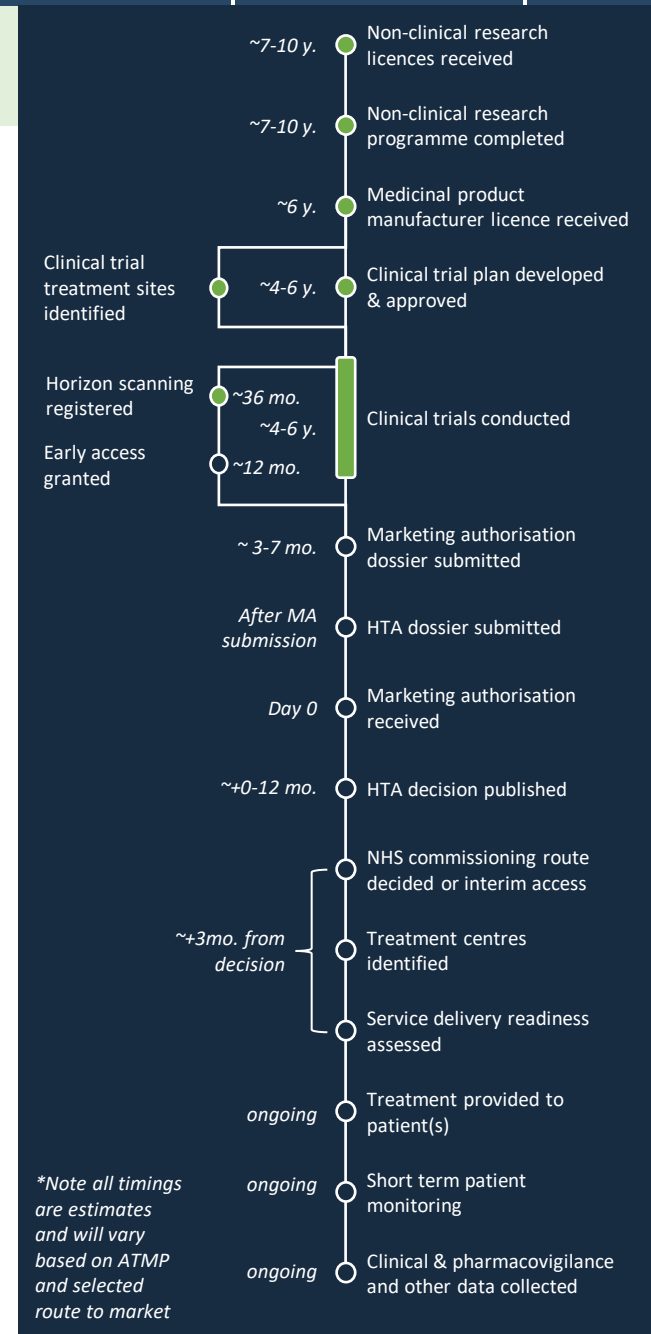
- Innovative Licensing and Access Pathway (ILAP) [optional]
- **International marketing authorisation coordination via Project Orbis [optional]**
- International marketing authorisation coordination via Access Consortium [optional]

## Overview

## To-do list

## Output

- For queries relating to project Orbis, contact the MHRA at Orbis-MHRA@mhra.gov.uk



## KEY TOPICS

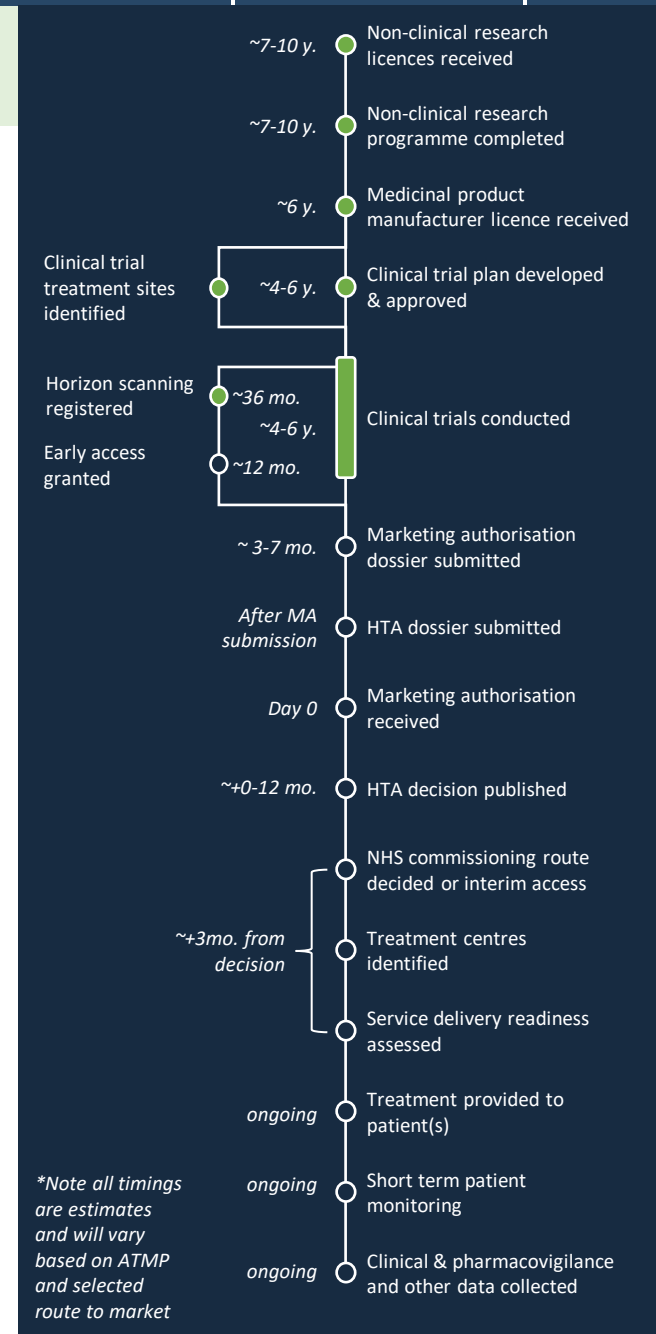


**Overview** | To-do list | Output

Developers can apply for a concurrent Marketing Authorisation submission and review in additional markets through the Access Consortium. There are a number of work sharing initiatives for different product types, so developers should review the guidance and ensure that it is relevant and applicable for their product.

Applicants for Access Consortium work sharing initiatives will still be required to submit their full Marketing Authorisation to the MHRA using their existing process, and will receive independent outcomes from participating countries. There are fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



1 What programmes are available to accelerate time to market?
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4 What reimbursement commercial arrangement options are available?

## KEY TOPICS



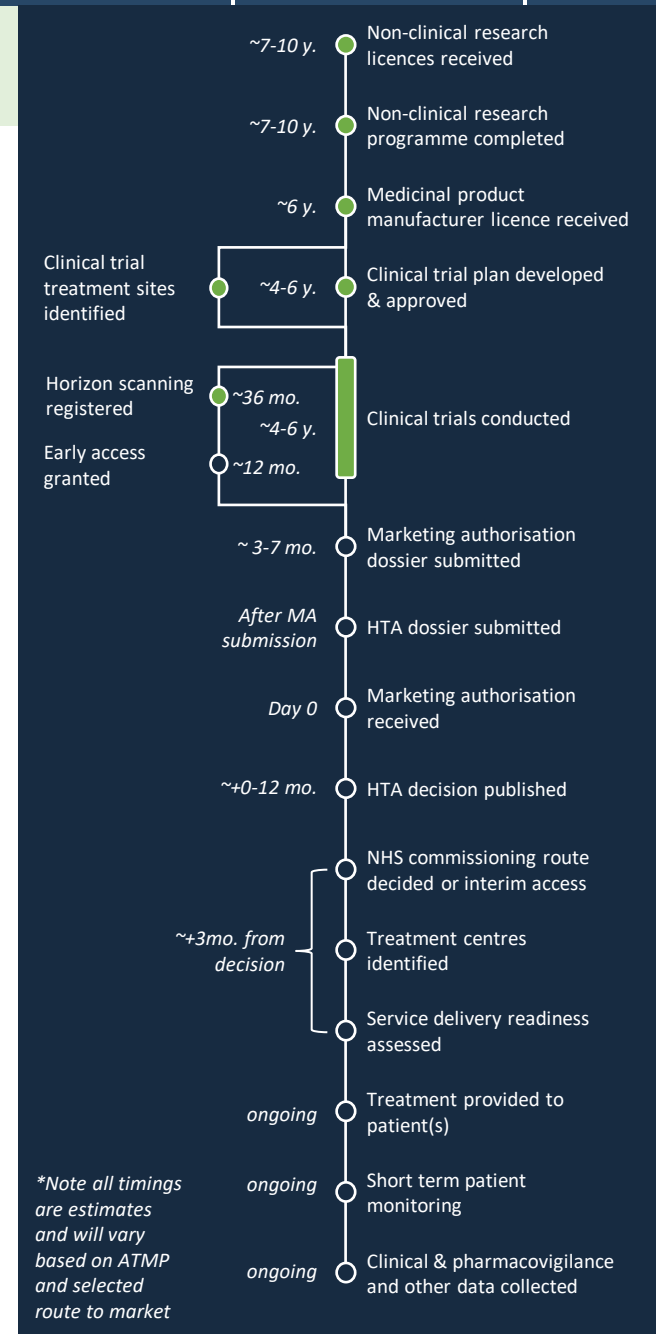
Overview | **To-do list** | Output

- Review Access Consortium guidance and determine if applicable for the product here
- Review the process for application in the New Active Substance (NAS) work sharing initiative here
- Express interest in the initiative using the expression of Interest (EOI) form available here, and submit to the MHRA (access-mhra@mhra.gov.uk) 3-6 months prior to MA submission
- Continue UK submission process along with concurrent submissions with participating countries (within 2 weeks of each other)

**When**

After completion of clinical trials and concurrent with UK Marketing Authorisation submission

Linked steps | Who is involved? | Best practices & tips

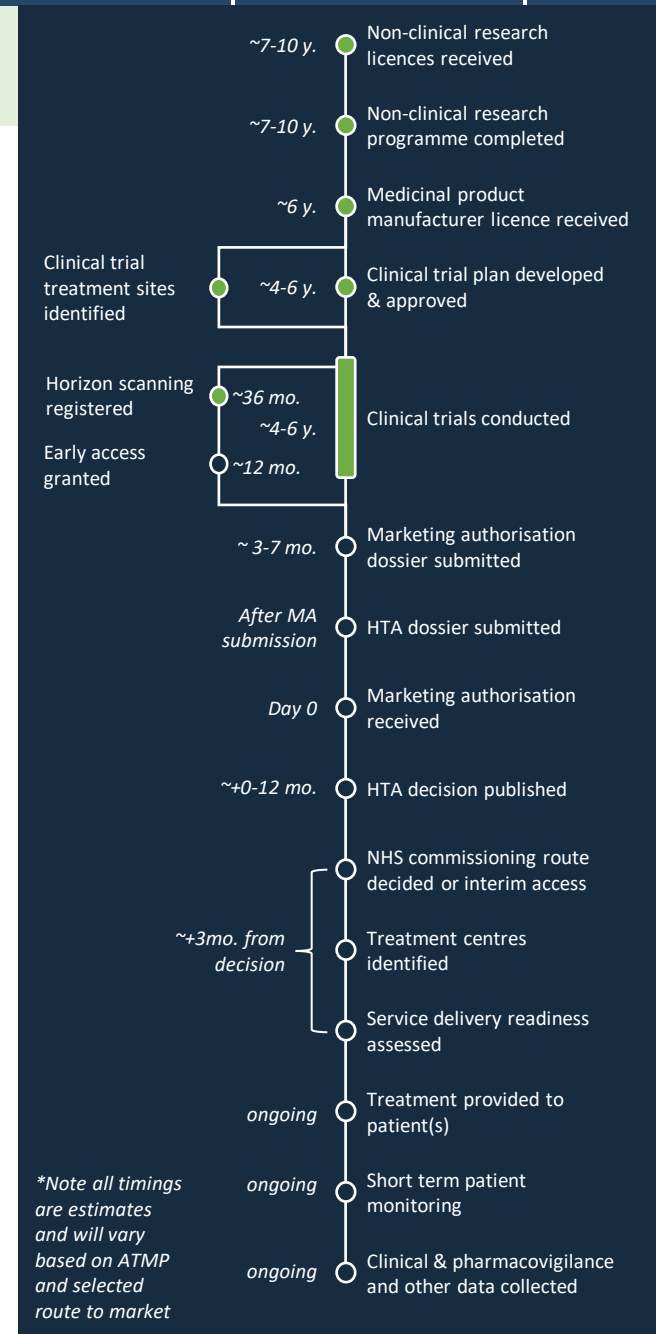


## KEY TOPICS



Overview | To-do list | **Output**

- Co-ordinated review of Marketing Authorisation application
- Marketing Authorisation decision from all participating Access consortium countries



## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

## Overview

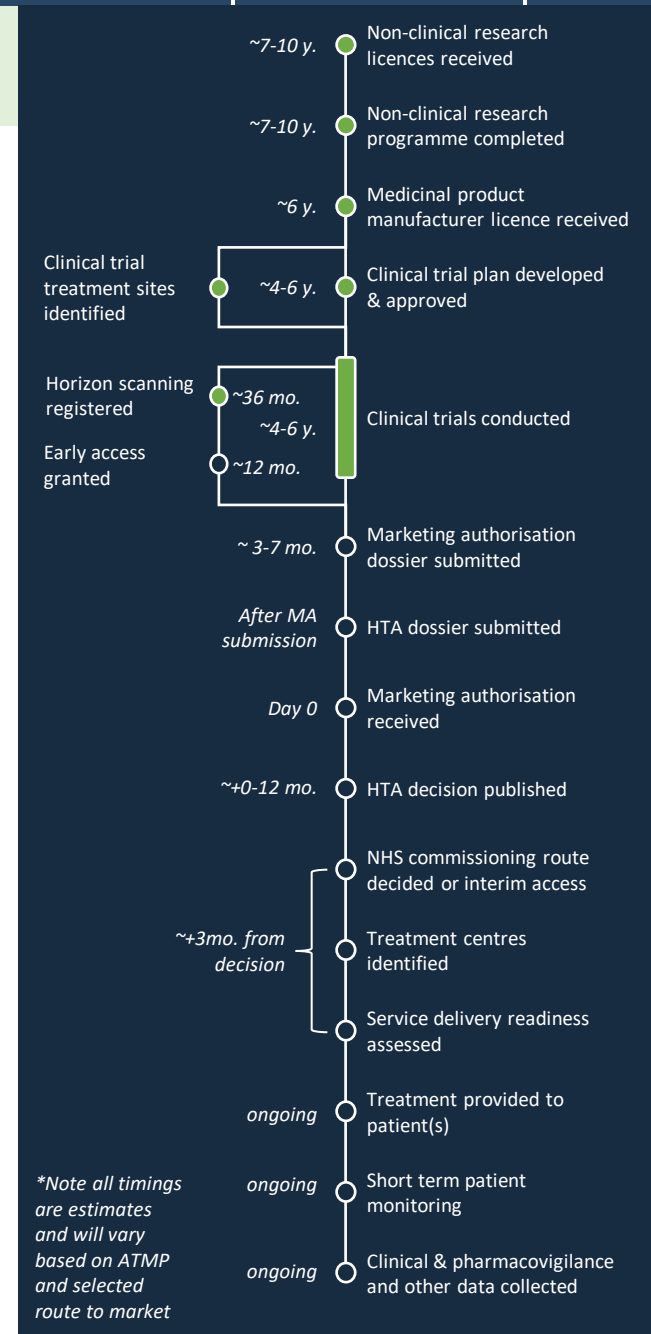
## To-do list

## Output

Marketing Authorisation submission

Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

## Overview

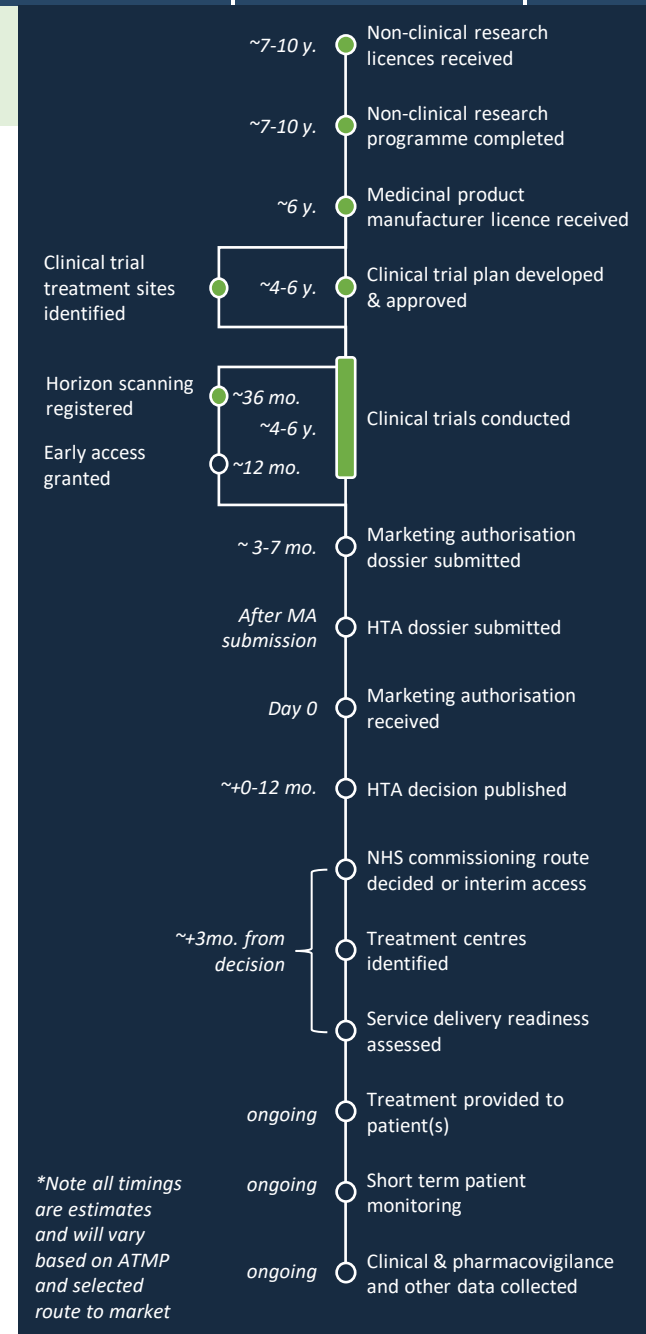
## To-do list

## Output

- ATMP developer
- MHRA

Access Consortium participating countries:

- TGA (Australia)
- Health Canada (Canada)
- HSA (Singapore)
- Swissmedic (Switzerland)



## KEY TOPICS

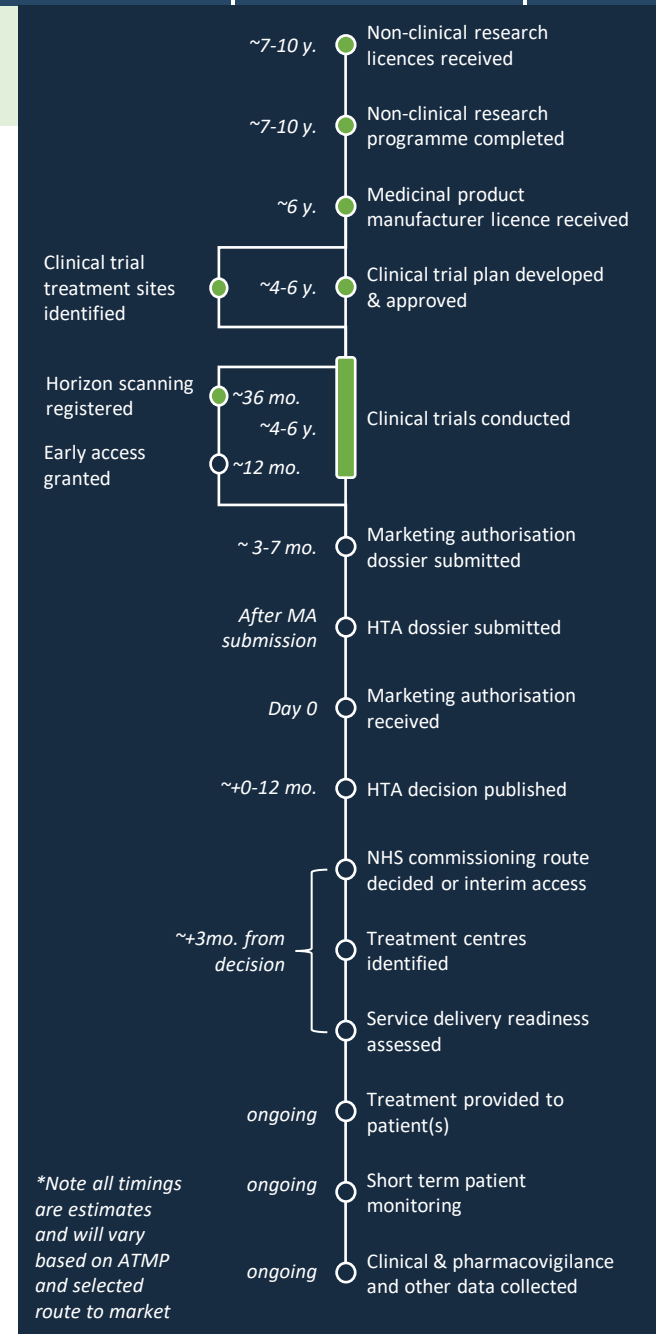
- Innovative Licensing and Access Pathway (ILAP) [optional]
- International marketing authorisation coordination via Project Orbis [optional]
- **International marketing authorisation coordination via Access Consortium [optional]**

## Overview

## To-do list

## Output

- For queries relating to Access Consortium Work Sharing Initiatives, contact the MHRA at access-mhra@mhra.gov.uk



## KEY TOPICS

- **Promising Innovative Medicine designation [optional]**
- EAMS scientific opinion [optional]

**Overview** | To-do list | Output

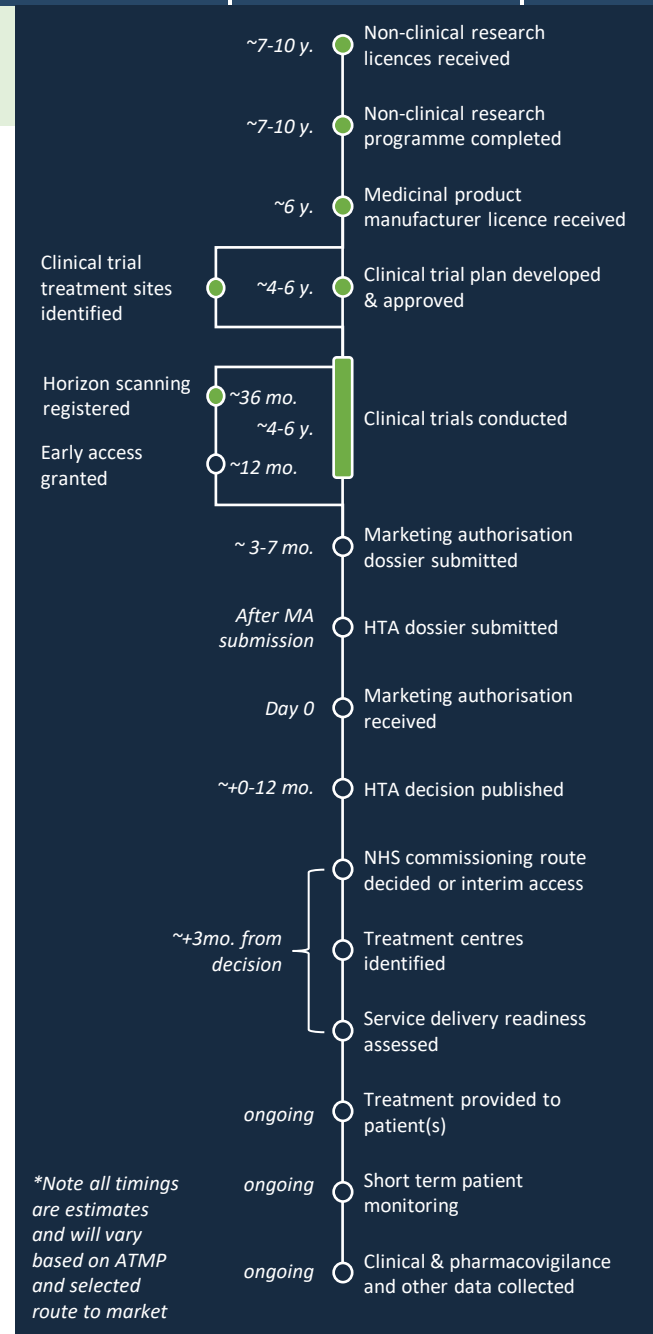
A Promising Innovative Medicine (PIM) designation is an early indication that a medicinal product is a promising candidate for the Early Access to Medicines Scheme (EAMS), intended for the treatment, diagnosis or prevention of a life-threatening or seriously debilitating condition with the potential to address an unmet medical need.

The PIM designation will be issued after an MHRA scientific designation meeting on the basis of non-clinical and clinical data available on the product, in a defined disease area. Following designation, the applicant is expected to complete a clinical development programme within a reasonable time period, in order to continue with an application under the EAMS. There are fees involved for this process.

Once the MHRA issue PIM designation, they will disclose the designation to NICE and NHSE. The NICE Office for Market Access (OMA) offers all companies with a PIM the opportunity to have a safe harbour engagement with NICE and NHSE (before the day 45 preliminary scientific opinion) to explore the developer's plans for the EAMS period in terms of operational delivery, feasibility of data collection, future HTA challenges and commercial options.

Note: in Scotland, the Area Drug and Therapeutics Committee Collaborative (ADTCC) and SMC invite all companies with a medicine with PIM status to attend a meeting to discuss operational delivery of EAMS and impact on future HTA.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

**Promising Innovative Medicine designation [optional]**

EAMS scientific opinion [optional]

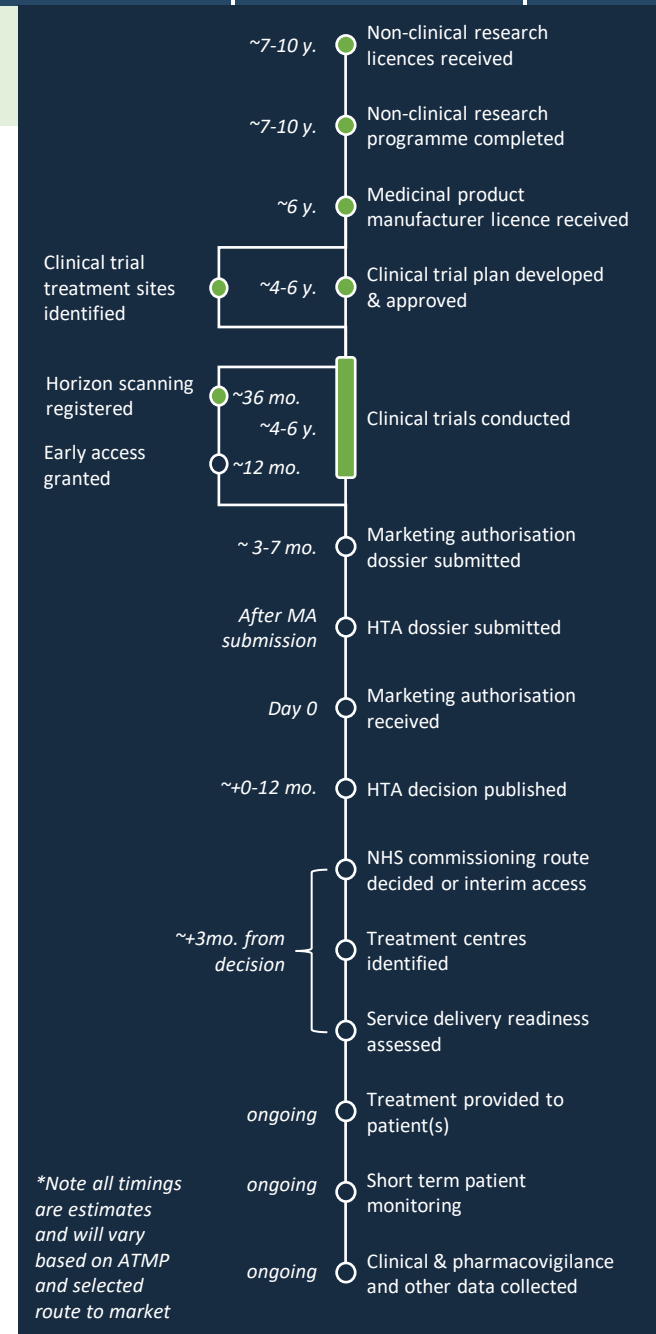
Overview | **To-do list** | Output

- Review the PIM designation guidance from the MHRA here
- To apply for a PIM designation submit the PIM application form here and send it to eams@mhra.gov.uk
  - Further information from the MHRA on the PIM/EAMS process can be found here
- Following PIM designation, engage with NHSE (and SMC if applicable) to conduct resource impact model and advance service impact assessment to support early access to ATMP (if applicable)
- Request a meeting with NICE's Office for Market here

**When**

Once Phase I or II clinical trial data are available and developer intention to seek Marketing Authorisation has been decided

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- **Promising Innovative Medicine designation [optional]**
- EAMS scientific opinion [optional]

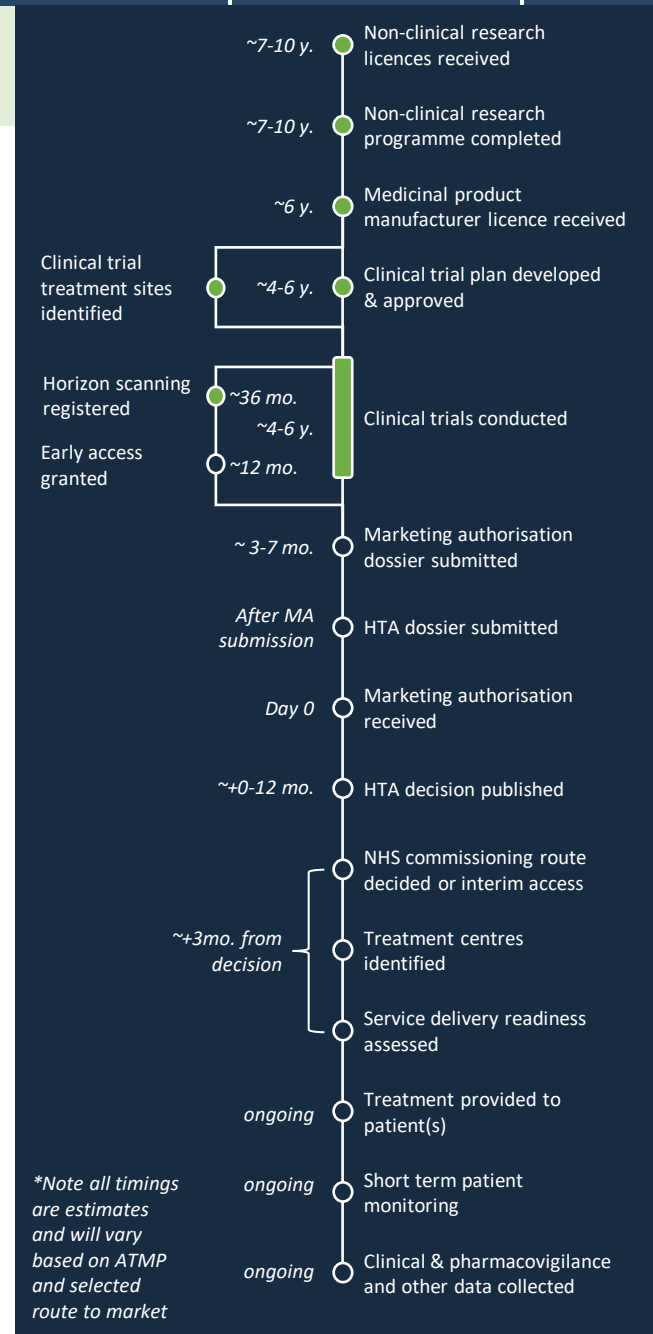
## Overview

- PIM designation

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

- **Promising Innovative Medicine designation [optional]**
- EAMS scientific opinion [optional]

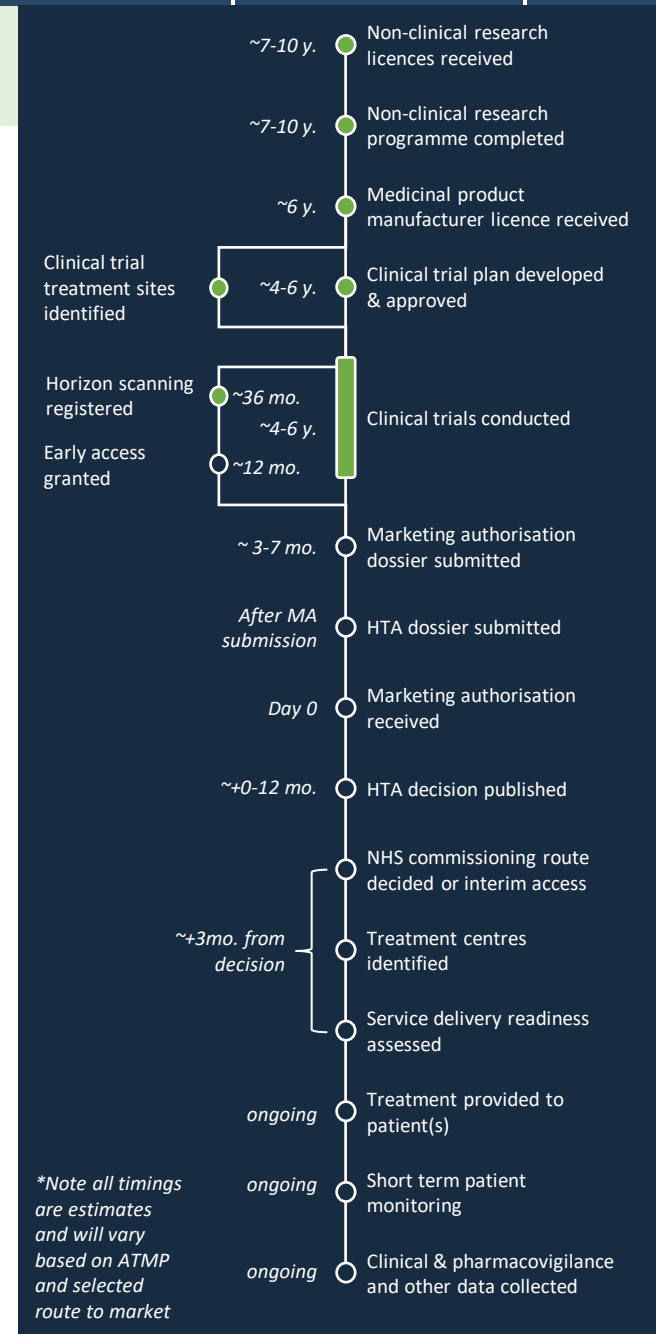
## Overview

## To-do list

## Output

- Marketing Authorisation submission
- Innovative Licensing and Access Pathway (ILAP) [optional]
- EAMS scientific opinion [optional]
- Early advice on Market Access process [optional]

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- **Promising Innovative Medicine designation [optional]**
- EAMS scientific opinion [optional]

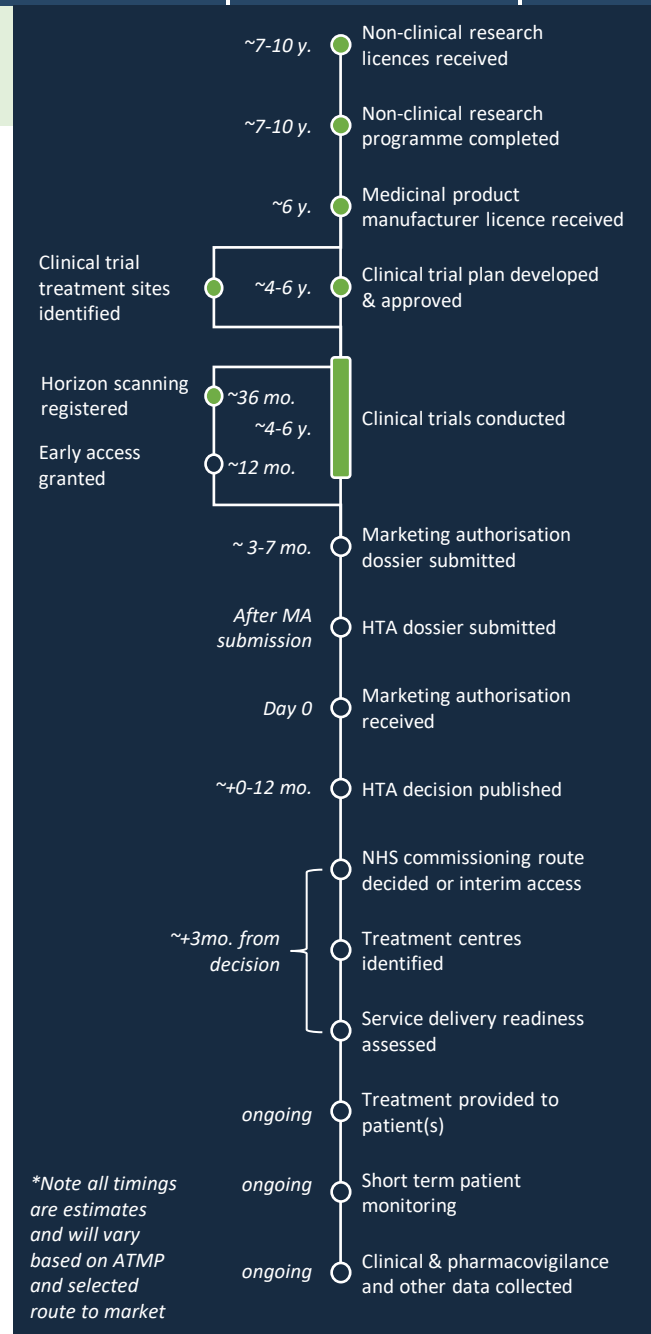
## Overview

## To-do list

## Output

- ATMP developer
- MHRA

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

- **Promising Innovative Medicine designation [optional]**
- EAMS scientific opinion [optional]

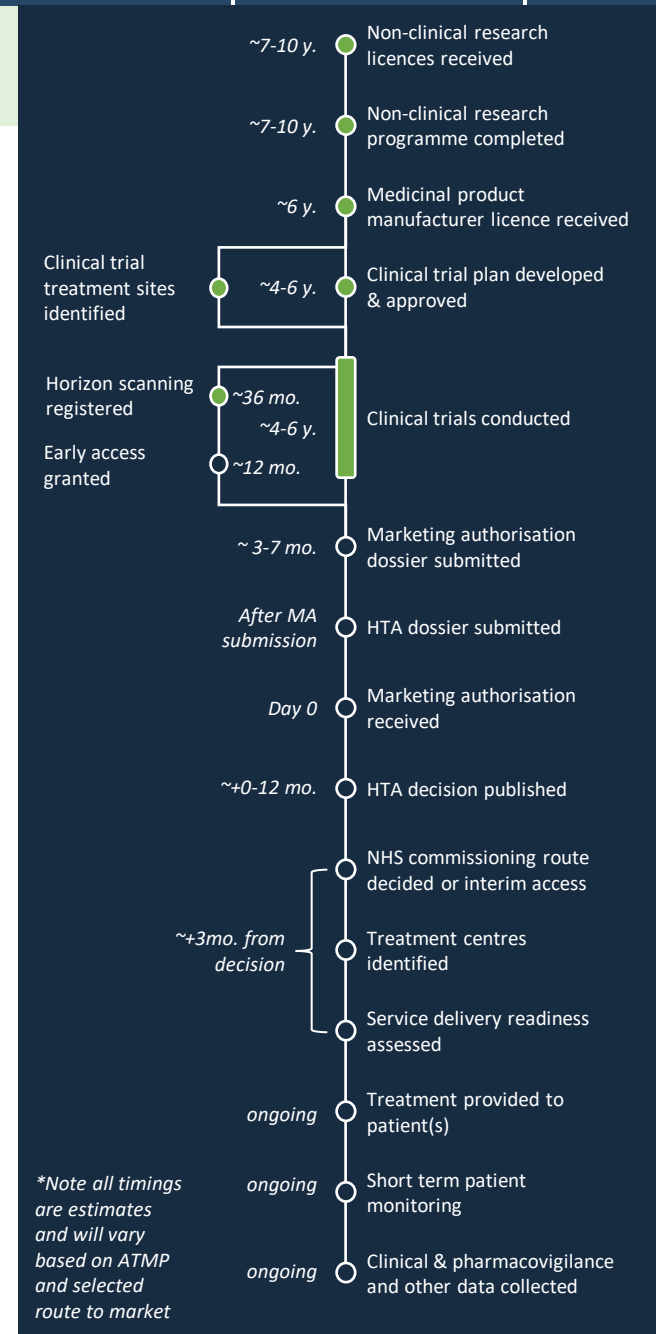
## Overview

## To-do list

## Output

- Assess the resource impact of providing early access with NHSE as early as possible to understand feasibility and likelihood of inclusion & success along the early access pathway
- When assessing resource impact, the overall financial impact should be considered, including infrastructure costs, resources, service delivery and service disruption

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS



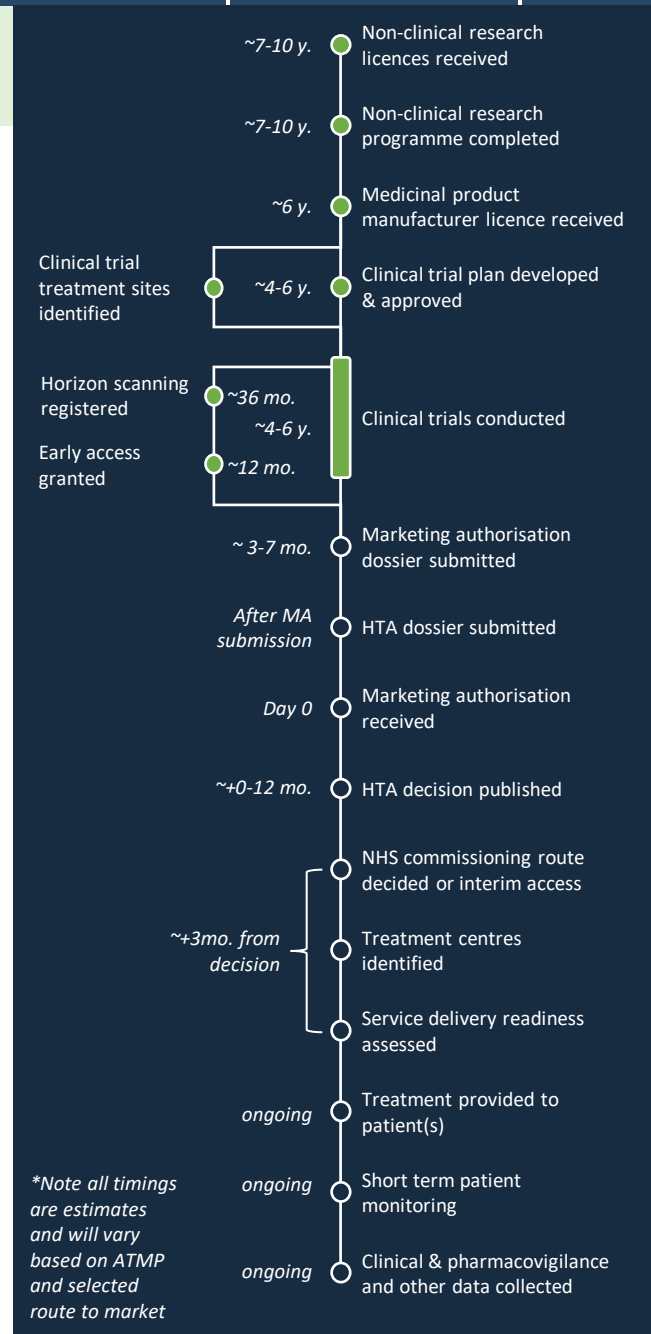
Overview | To-do list | Output

The Early Access to Medicines Scheme (EAMS) helps to give people with life threatening or seriously debilitating conditions early access to new medicines that do not yet have a marketing authorisation but where there is a clear unmet medical need. EAMS also provides developers with additional data generation opportunities in the target patient population and improve clinician experience with the product prior to launch.

By promoting early engagement between companies, and key Accelerated Access Collaborative (AAC) partners including MHRA, NICE and NHS England and NHS Improvement, EAMS also helps to create a smoother route to market for new treatments.

Developers must complete and submit an EAMS dossier to MHRA and attend a pre-submission meeting. The NICE Office for Market Access offers developers the opportunity to have a supplementary meeting with NICE to discuss their data collection plans during the EAMS period, in order to help ensure the developer is well prepared for a potential Technology Appraisal or Highly Specialised Technologies evaluation. A positive EAMS scientific opinion is granted by MHRA and enables patients to receive drugs ~12-18 months prior to marketing authorisation being granted. Developers will be required to provide the treatment to the NHS for free during the EAMS period. There are fees involved for this process.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

Promising Innovative Medicine designation [optional]
**EAMS scientific opinion [optional]**

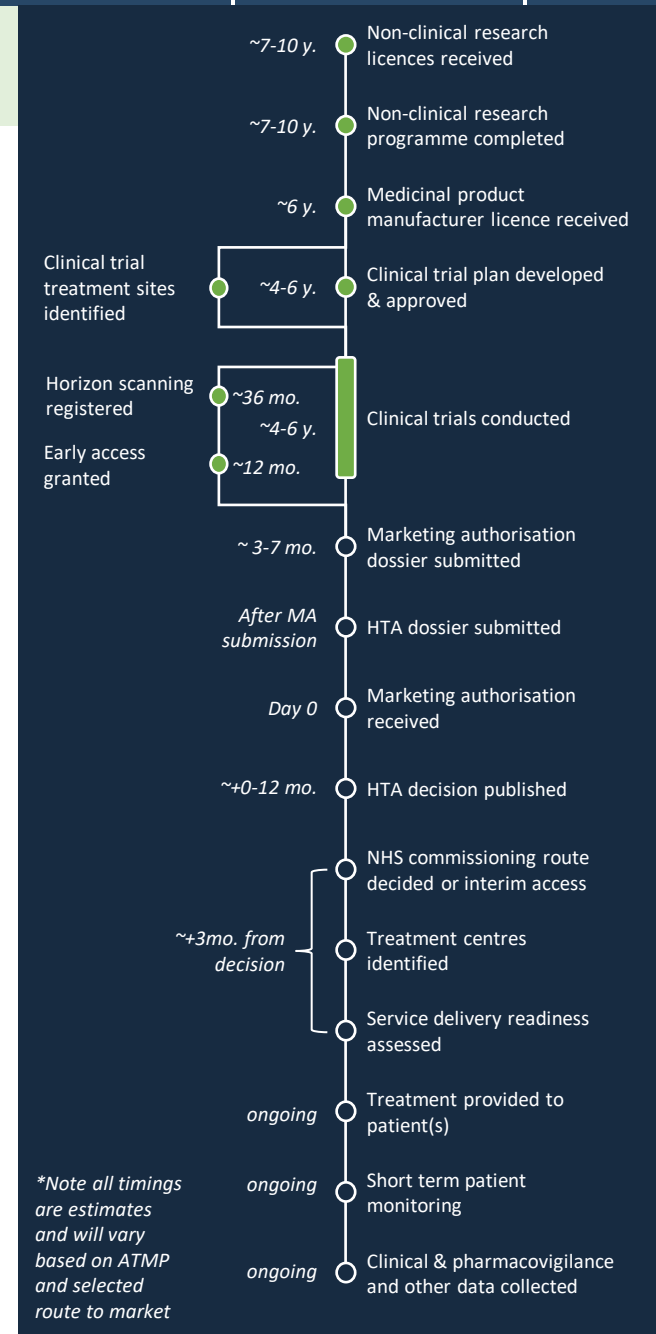
Overview | **To-do list** | Output

- Review MHRA guidance on EAMS here
- Complete scientific opinion application form here
  - Developers should also include Risk Management Plan, budget and service impact documentation, and pharmacovigilance system master file (PSMF) summary
- Submit EAMS dossier to MHRA to apply for scientific opinion to eams@mhra.gov.uk
- Request pre-submission meeting with MHRA here and attend meeting
- Request a meeting with NICE's Office for Market here
- Prepare transition to MA/exit plan for EAMS scheme
- [Scotland only] Complete operational guidance templates provided by ADTCC to assist NHS Boards in Scotland with local management of access to medicines via EAMS

### When

- After receipt of PIM designation
- EAMS scientific opinion lasts for 1 year and lapses at the time of granting of MA

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

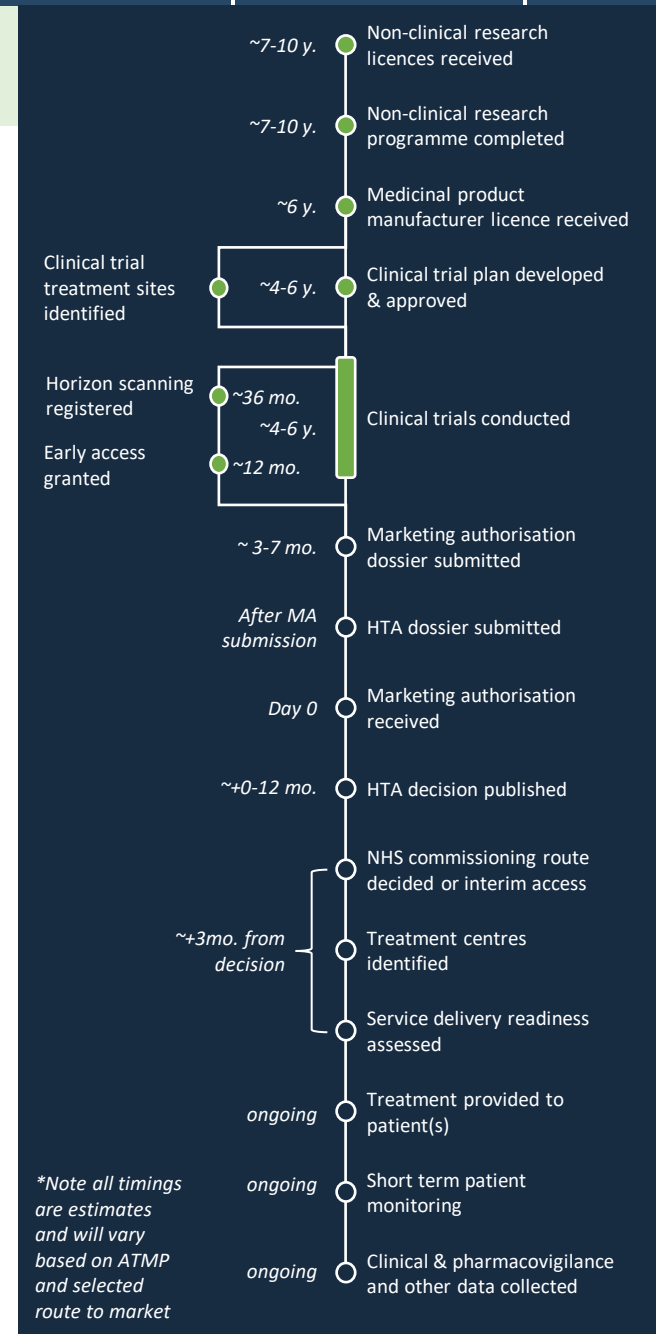
Promising Innovative Medicine designation [optional]

**EAMS scientific opinion [optional]**

Overview | To-do list | **Output**

- EAMS scientific opinion and notification of NHSE, NHSW, NHS Scotland, NICE, SMC, etc. by MHRA
- Public Assessment Report published by MHRA
- Developer provision of ATMP free of charge pre-MA (and post-MA for patients receiving ongoing treatment)
- Commissioning for drug with EAMS designation, after EAMS period ends
- RWD collection
- Transition plan for post-MA (including exit plan)

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

Promising Innovative Medicine designation [optional]

**EAMS scientific opinion [optional]**

## Overview

Routine commissioning

Health Technology Assessment Technology Appraisal

Health Technology Assessment Highly Specialised Technologies evaluation

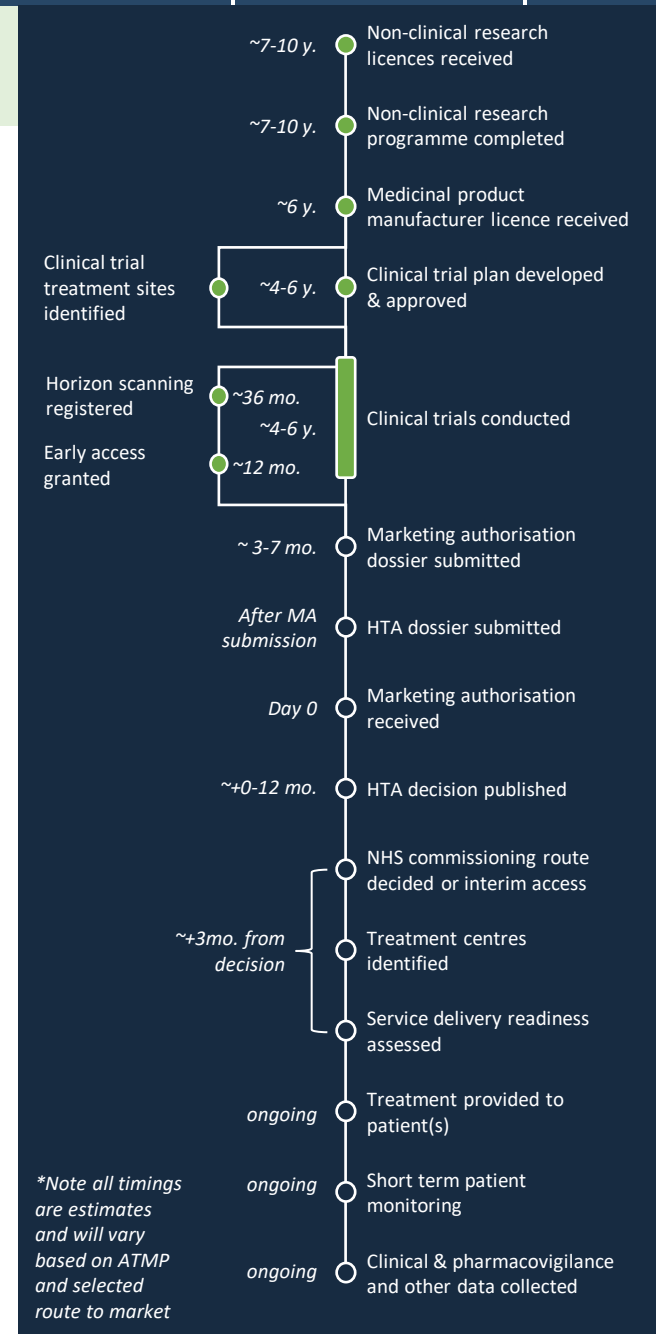
Marketing Authorisation submission

Early advice on Market Access process [optional]

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

Promising Innovative Medicine designation [optional]

**EAMS scientific opinion [optional]**

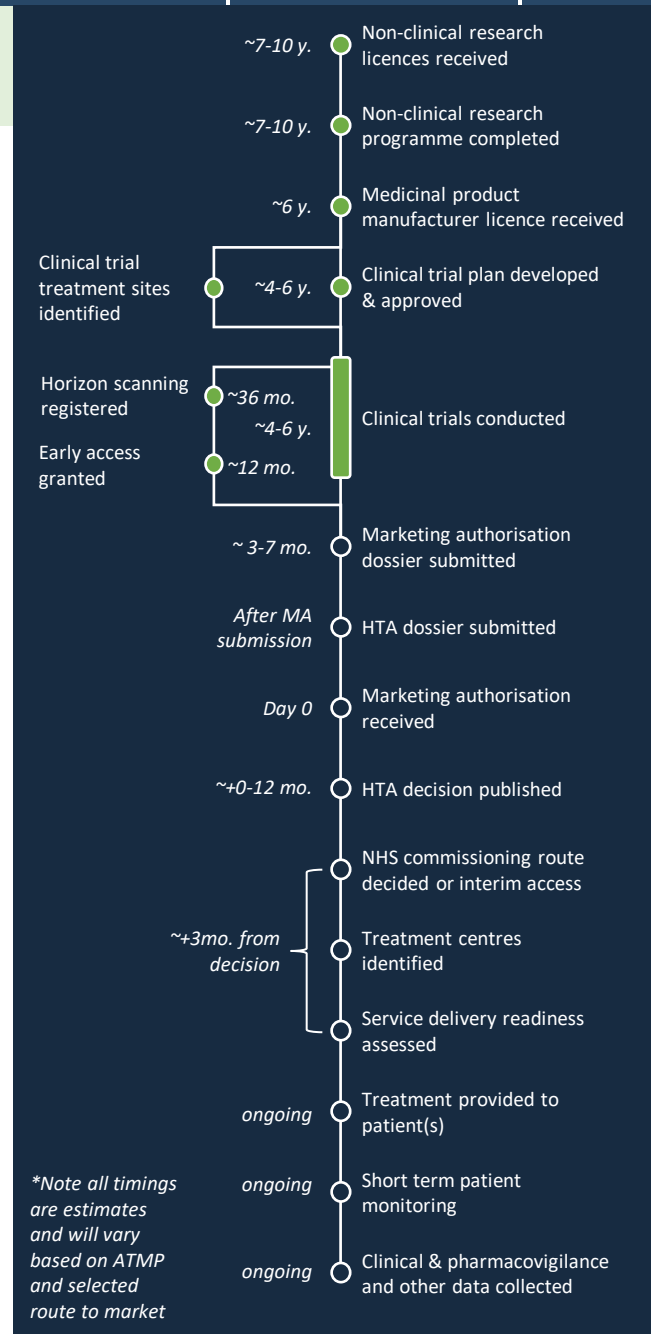
## Overview

## To-do list

## Output

- ATMP developer
- MHRA
- NICE
- NHS commercial team

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

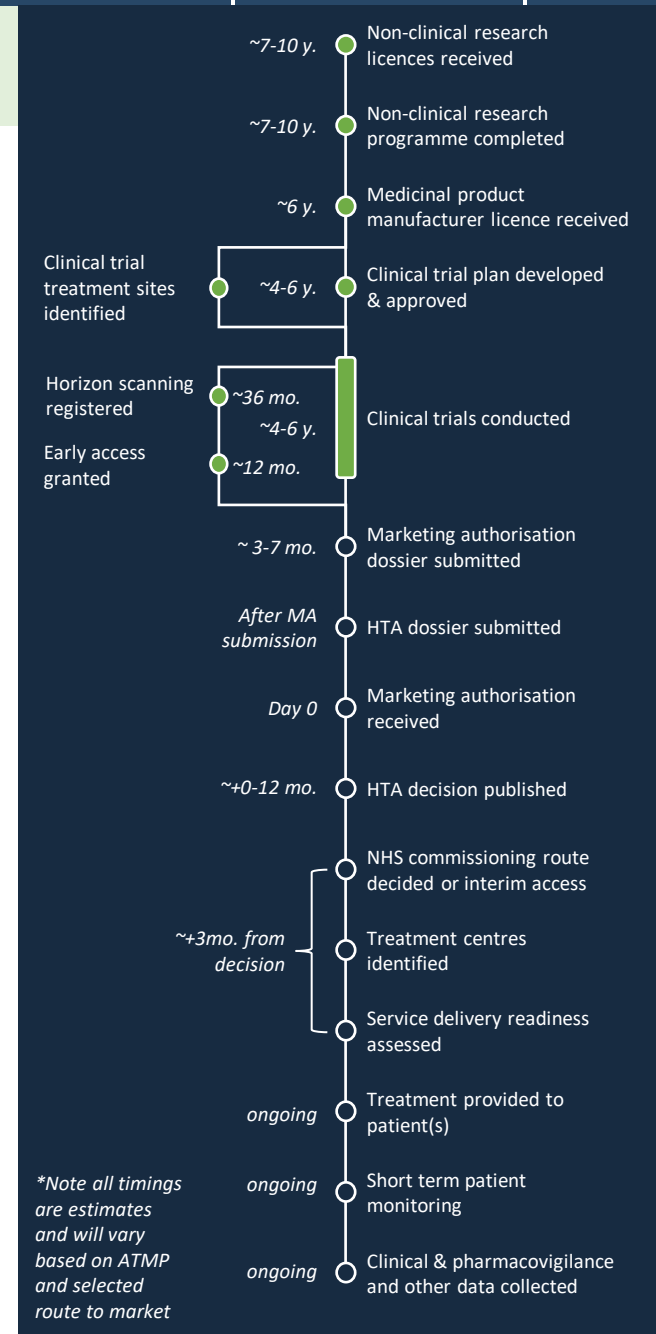
Promising Innovative Medicine designation [optional]

**EAMS scientific opinion [optional]**

Overview | To-do list | Output

- Developers should consider exit point from early access and commissioning setting before entering the scheme, and should consider whether their ATMP is commercially suited for EAMS, particularly if a one-off treatment or requires significant service re-design.

**Linked steps** | **Who is involved?** | **Best practices & tips**



## KEY TOPICS

- **Early advice on Market Access process [optional]**
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation

**Overview** | To-do list | Output

ATMP developers can engage early with healthcare system partners to get advice on market access processes.

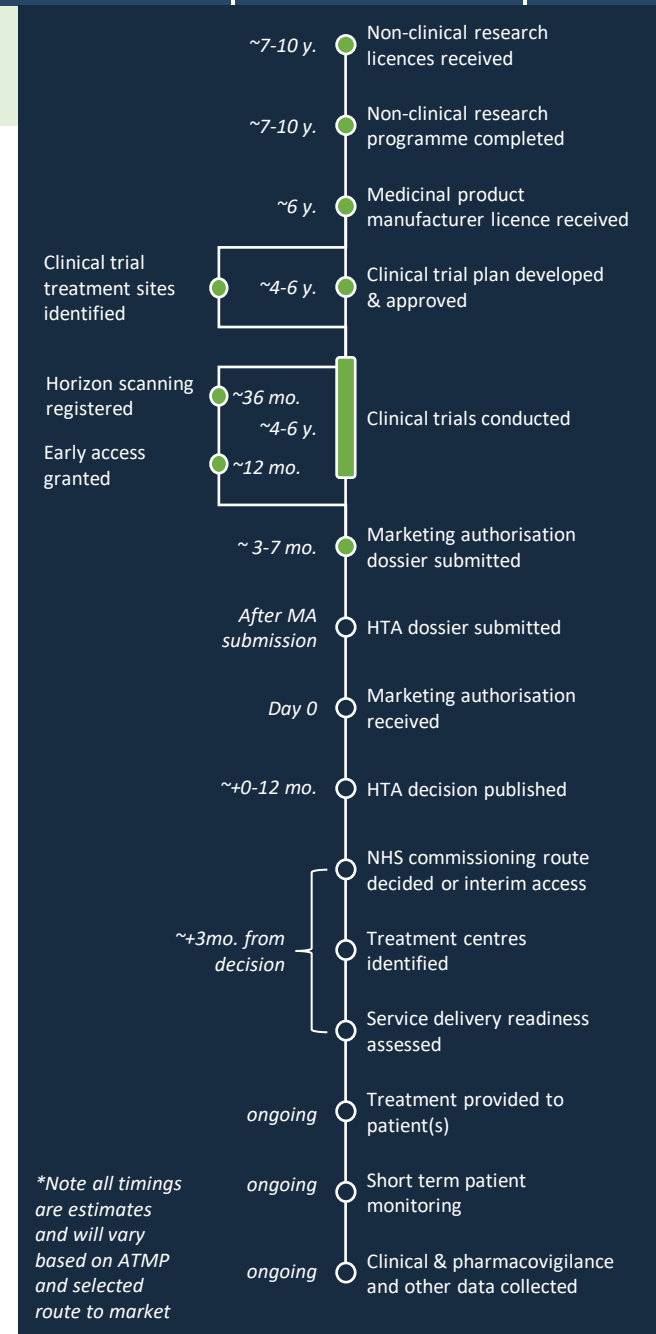
This may be done through a number of routes, including but not limited to:

- Requesting advice and a safe harbour engagement with the NICE Office for Market Access
- Requesting and attending Cell and Gene Therapy Catapult Commercial Readiness Clinics
- Requesting advice on setting up a Developer-led Advisory Board

Developers can also request a commercial or clinical surgery with NHS England to facilitate further targeted discussions. Commercial surgeries are often used to discuss a complex PAS or commercial agreement, whereas clinical surgeries allow for interfacing with the specialised commissioning team.

There may be fees involved for these services.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- **Early advice on Market Access process [optional]**
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation

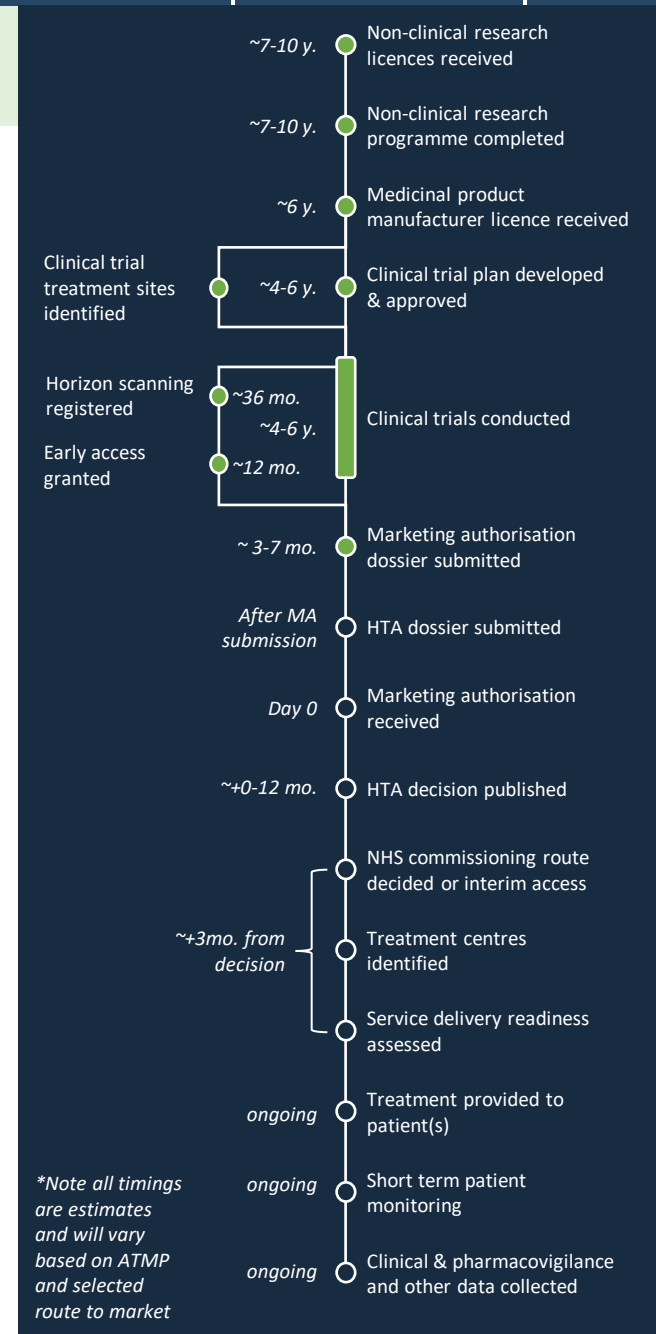
Overview | **To-do list** | Output

- Engage with external stakeholders to develop and tailor market access strategy
- Some examples of resources that may be useful are:
  - NICE's Office for Market Access information can be found here and a developer may request a meeting here
  - CGT Catapult Commercial Readiness Clinic information can be found here
  - General guidance on Advisory Boards from the ABPI can be found here

**When**

Prior to Health Technology Assessment submission

Linked steps | Who is involved? | Best practices & tips

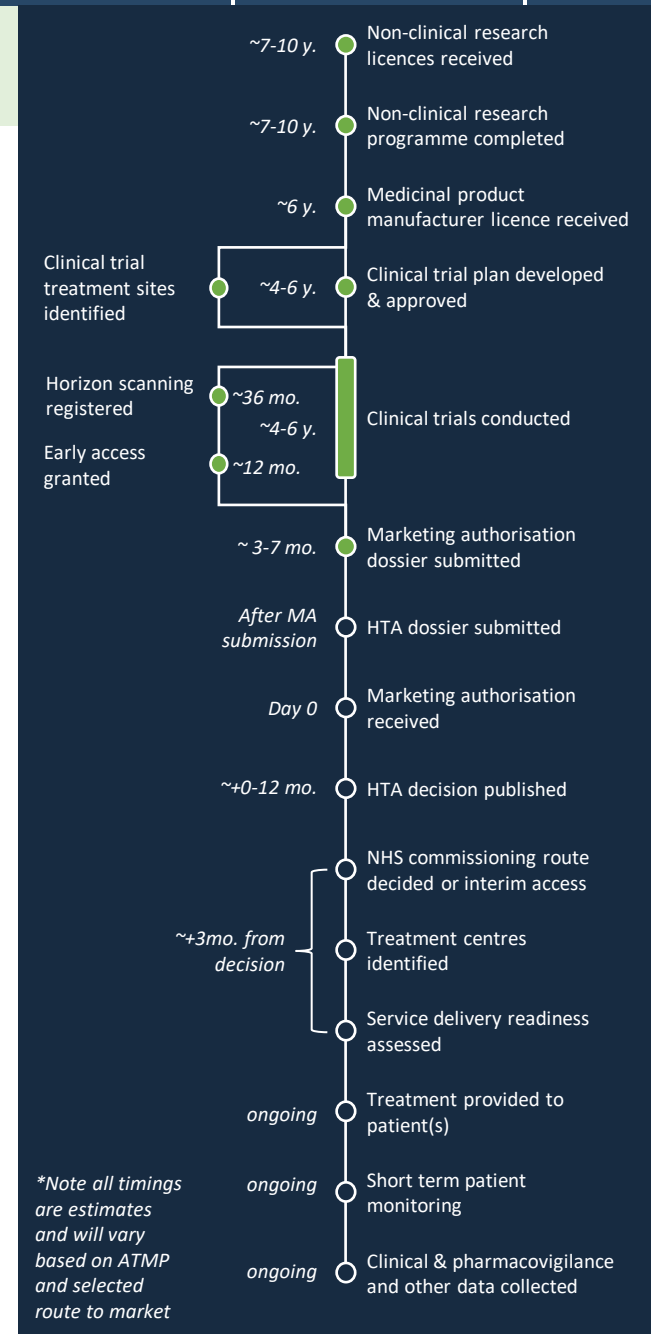


## KEY TOPICS

- **Early advice on Market Access process [optional]**
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation

Overview | To-do list | **Output**

- External advice/input to develop plan to bring product to market




Linked steps | Who is involved? | Best practices & tips

## KEY TOPICS

- **Early advice on Market Access process [optional]**
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation

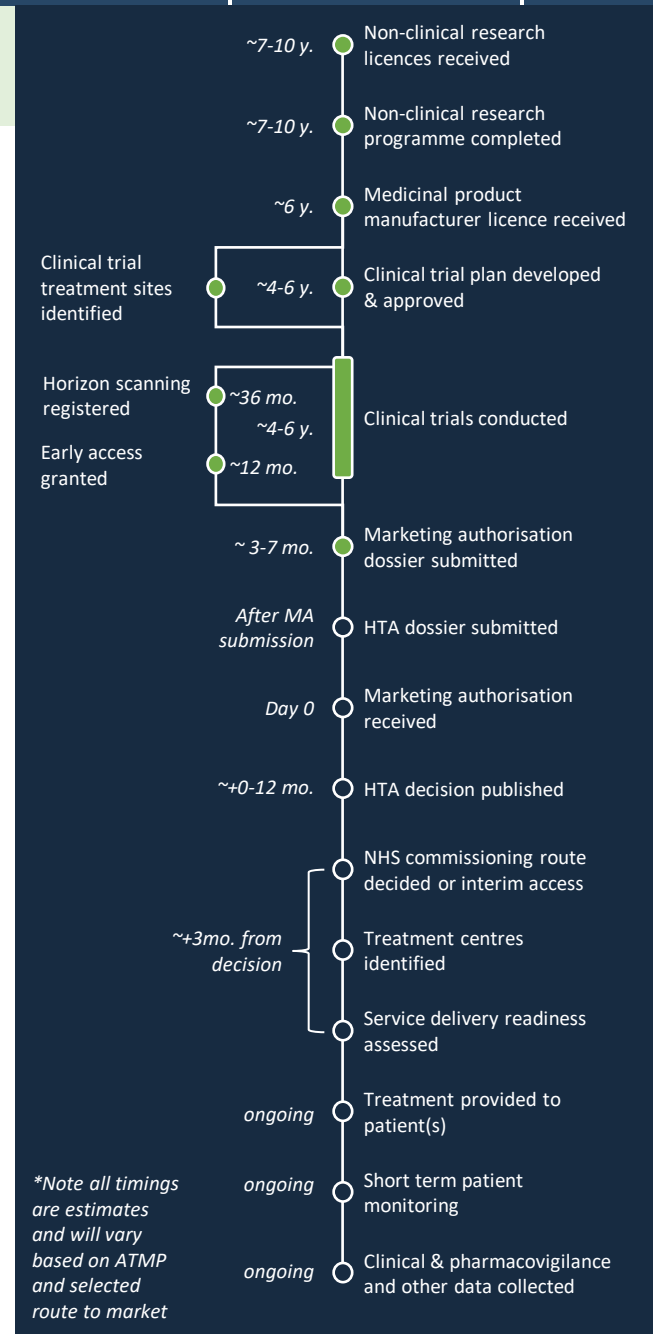
## Overview

## To-do list

## Output

- Marketing Authorisation submission
- Service delivery readiness
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation
- Promising Innovative Medicine designation [optional]
- Regulatory and/or scientific advice

**Linked steps** **Who is involved?** **Best practices & tips**



1 What programmes are available to accelerate time to market?

2 How can an ATMP obtain early access through EAMS?

3 What are the routes for ATMP reimbursement assessment?

4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

**Early advice on Market Access process [optional]**

Health Technology Assessment Technology Appraisal

Health Technology Assessment Highly Specialised Technologies evaluation

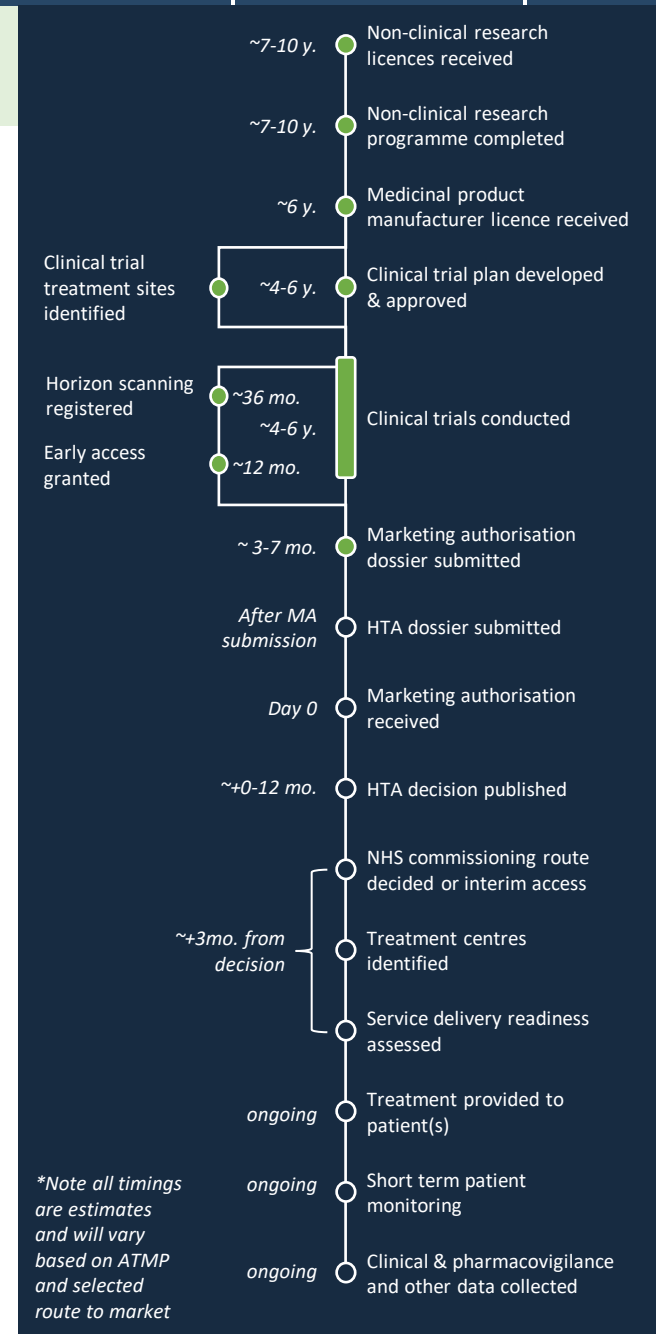
## Overview

## To-do list

## Output

- ATMP developer
- OMA (NICE)
- Cell and Gene Therapy Catapult
- NHS commercial team

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- **Early advice on Market Access process [optional]**
- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation

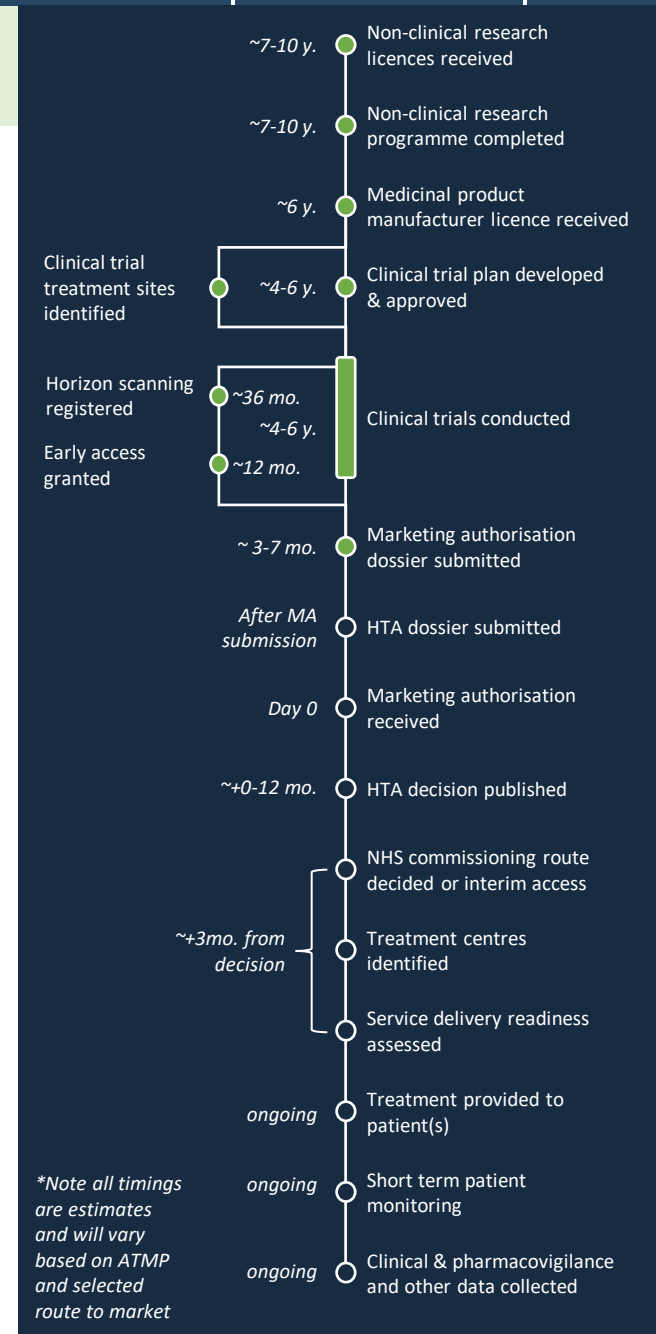
## Overview

## To-do list

## Output

- Consulting on scope details is important and should consider comparators used and intended NICE evaluation route

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

**Overview** | To-do list | Output

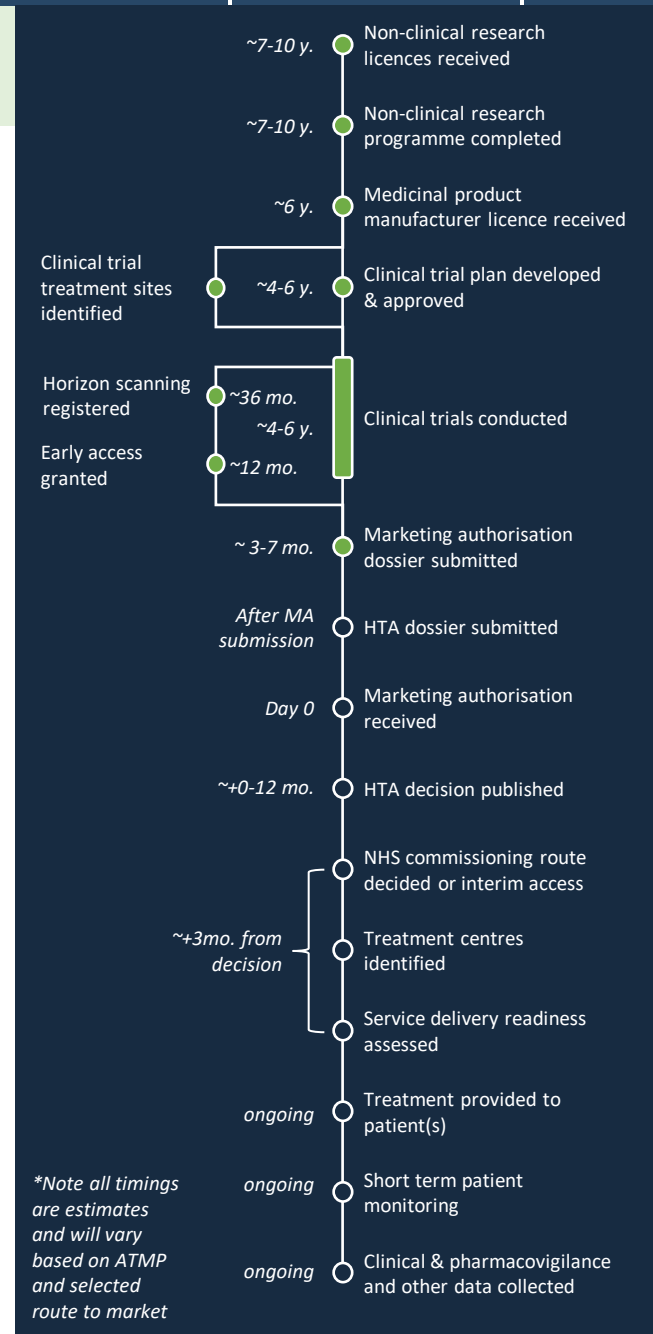
Prior to Developer submission, a number of activities will be completed by NICE:

- Ministerial referral of Appraisal topics
- Provisional evaluation topics chosen (this determines if HST or TA route is most appropriate for the product - further detail on how NICE does this can be found here)
- NICE will identify that the ATMP should be routed for highly specialised technology (HST) evaluation
- Scope preparation (this defines the disease, the patients eligible and the technologies covered by the appraisal and will include input from patient groups/PPI)
    - This also defines the PICO parameters (patient/population, intervention, comparison and outcomes) that the developer and ERG should follow
- Identification and briefing of consultees and commentators

Once these steps are completed, developers should prepare and submit their evidence dossiers, which may include a commercial arrangement, along with a budget impact test assessment and attend an appraisal committee meeting with NICE stakeholders.
During the evidence review process, developers will also need to respond to any requests for clarifications and/or additional analyses made by NICE or consultees/ experts.

There are fees involved for the HTA process.





## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

Overview | **To-do list** | Output

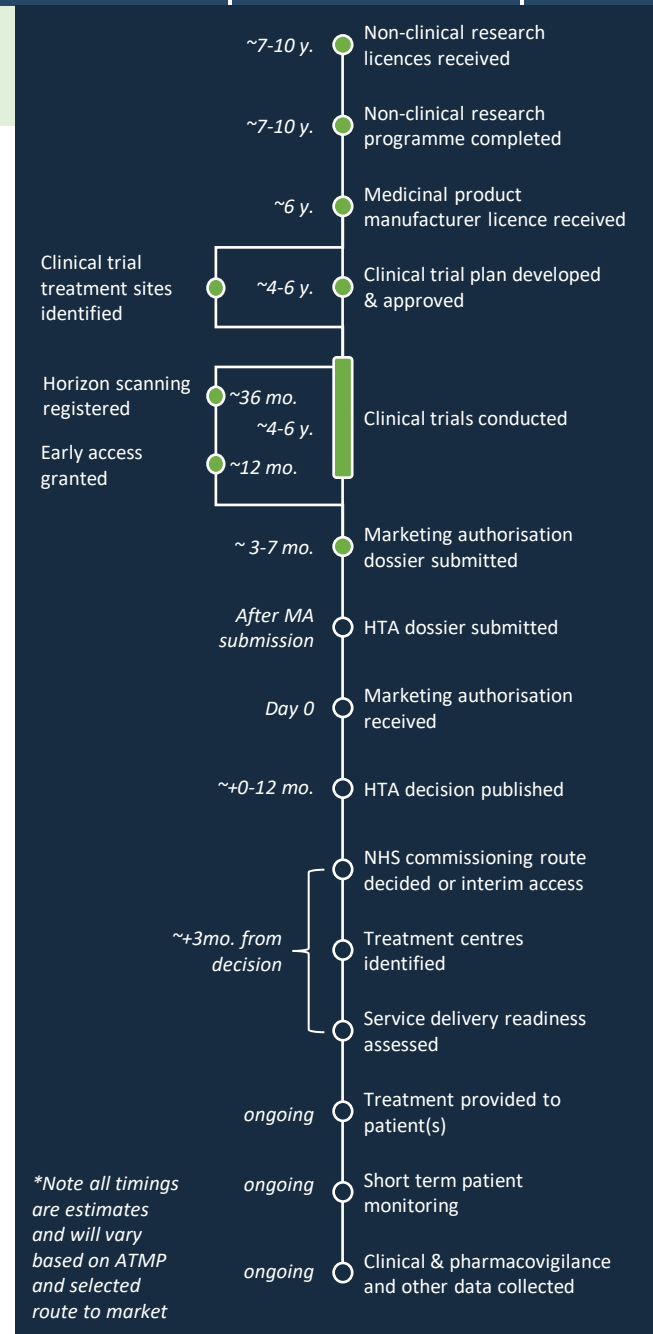
- Review NICE Technology Appraisal process and guidance here
  - Guidance from the ATTC on preparing for HTA for ATMPs can be found here
- Submit evidence to NICE along with (if required) commercial arrangement details using TA submission template which can be navigated to via the NICE guidance here
  - Refer to commercial arrangement topics below for details on requirements and approval
  - Guidance on economic modelling from EUNetHTA can be found here
  - Information on NICE's PRIMA service to healthcheck models used can be found here
- Complete budget impact assessment using NICE form here, further information can be found here
- Prepare for and attend appraisal committee meeting with NICE

**When**

- Developers should commence HTA process during MA application and aim for concurrent approvals of MHRA and NICE (subject to NICE capacity)

Note that NICE will not issue final guidance until UK MA has been received.

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

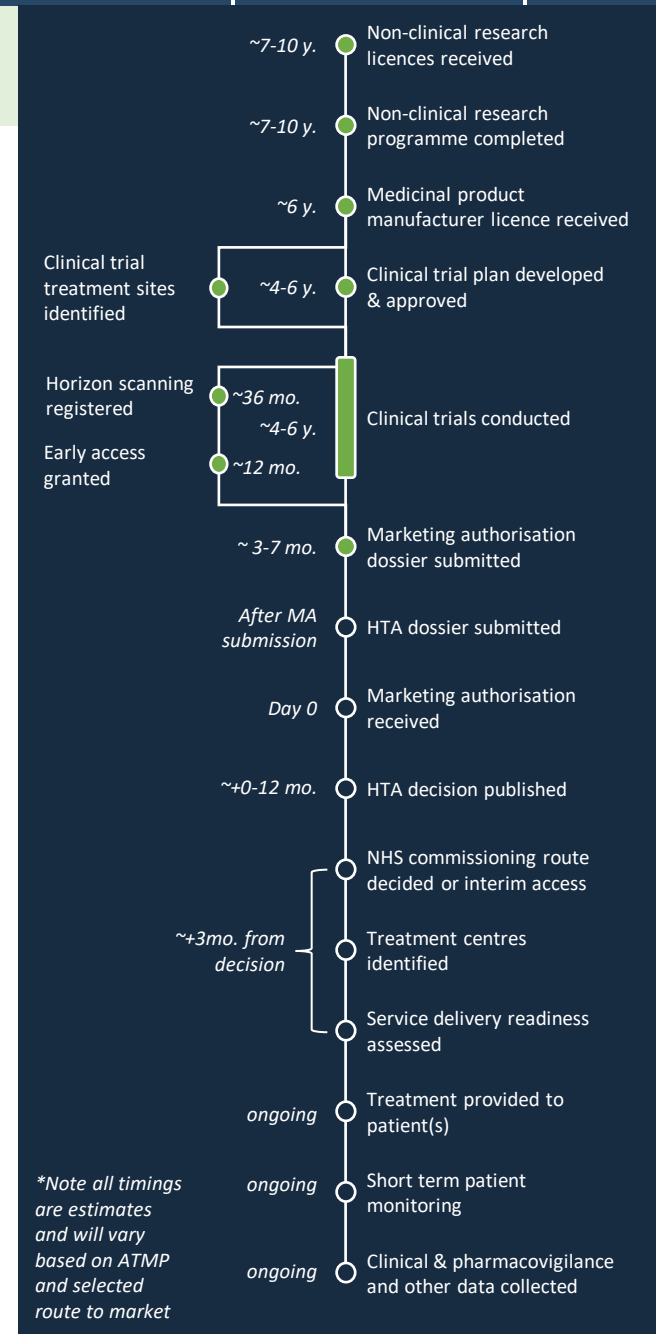


## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

Overview | To-do list | **Output**

- Evidence Review Group (ERG) assessment report
- Final appraisal document (FAD) following Appraisal committee and consultation
- NICE guidance issued with one of the following three recommendations:
  - Recommendation for routine commissioning
  - Recommendation for use with a Managed Access Agreement
  - Not recommended for routine commissioning




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

## Overview

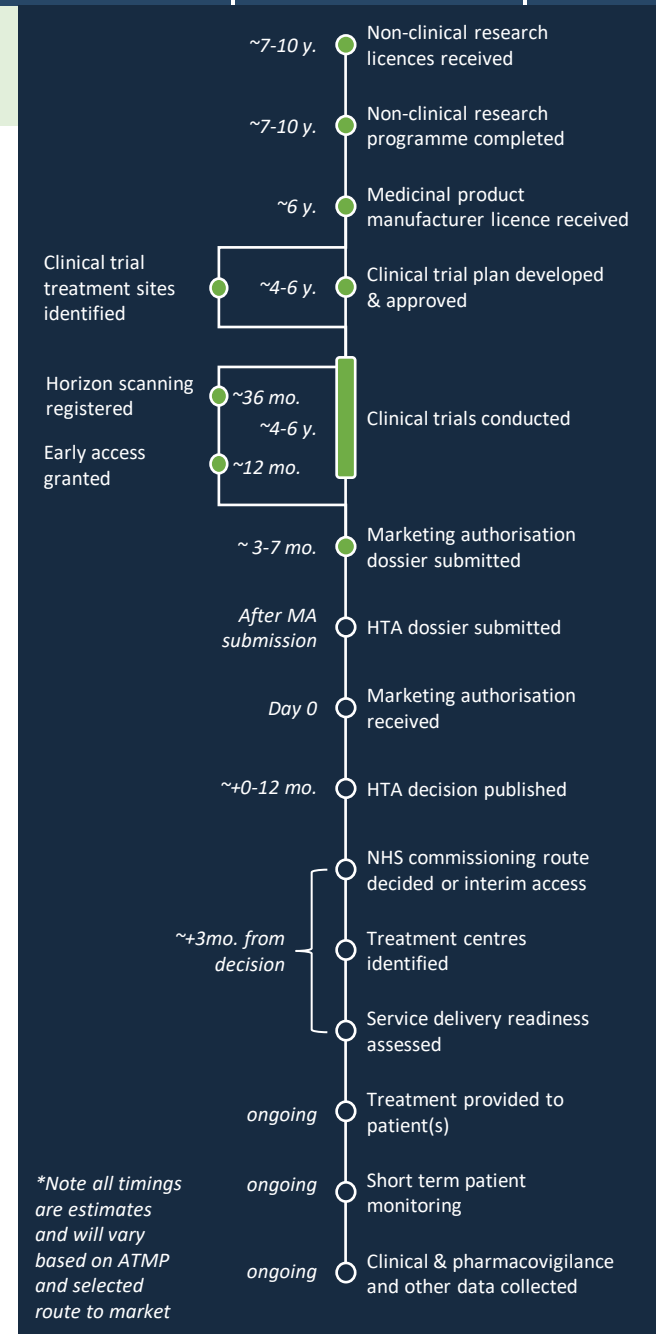
## To-do list

## Output

- Horizon scanning registration
- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]
- Service delivery readiness

Linked steps | Who is involved? | Best practices & tips

**Variation by devolved nation**



## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

## Overview

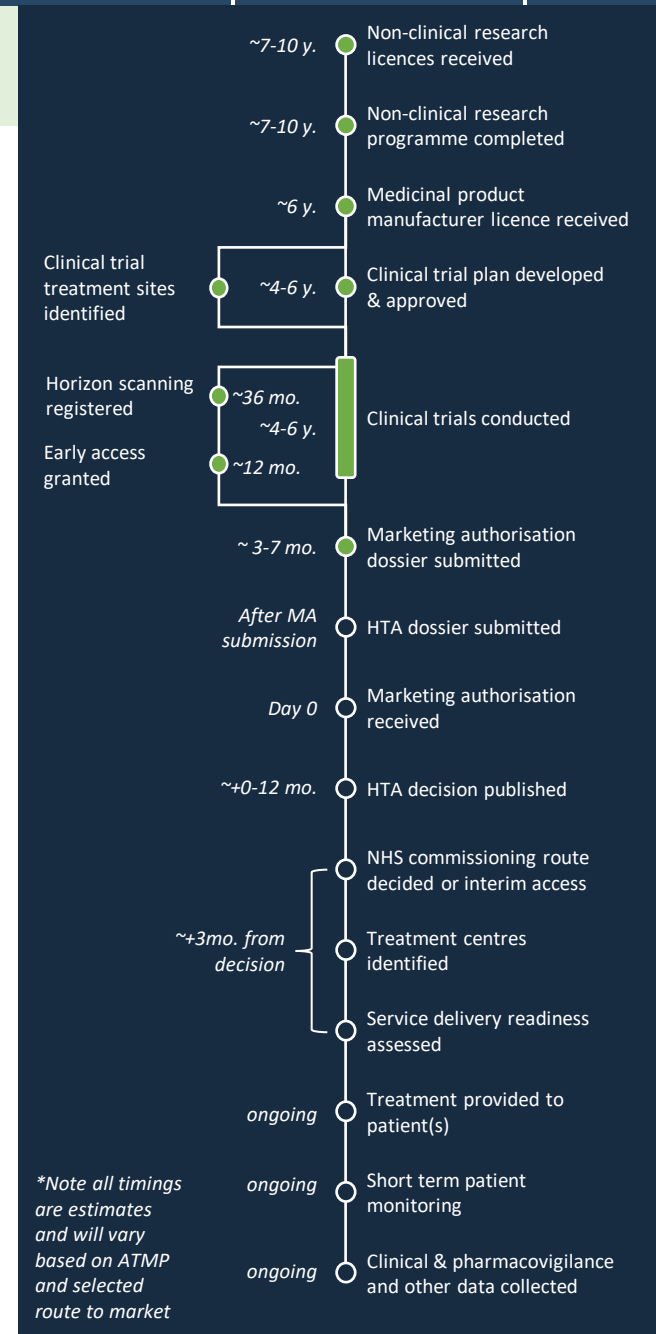
## To-do list

## Output

- ATMP developer
- NICE
- PPI
- NHSE

Linked steps | Who is involved? | Best practices & tips

Variation by devolved nation



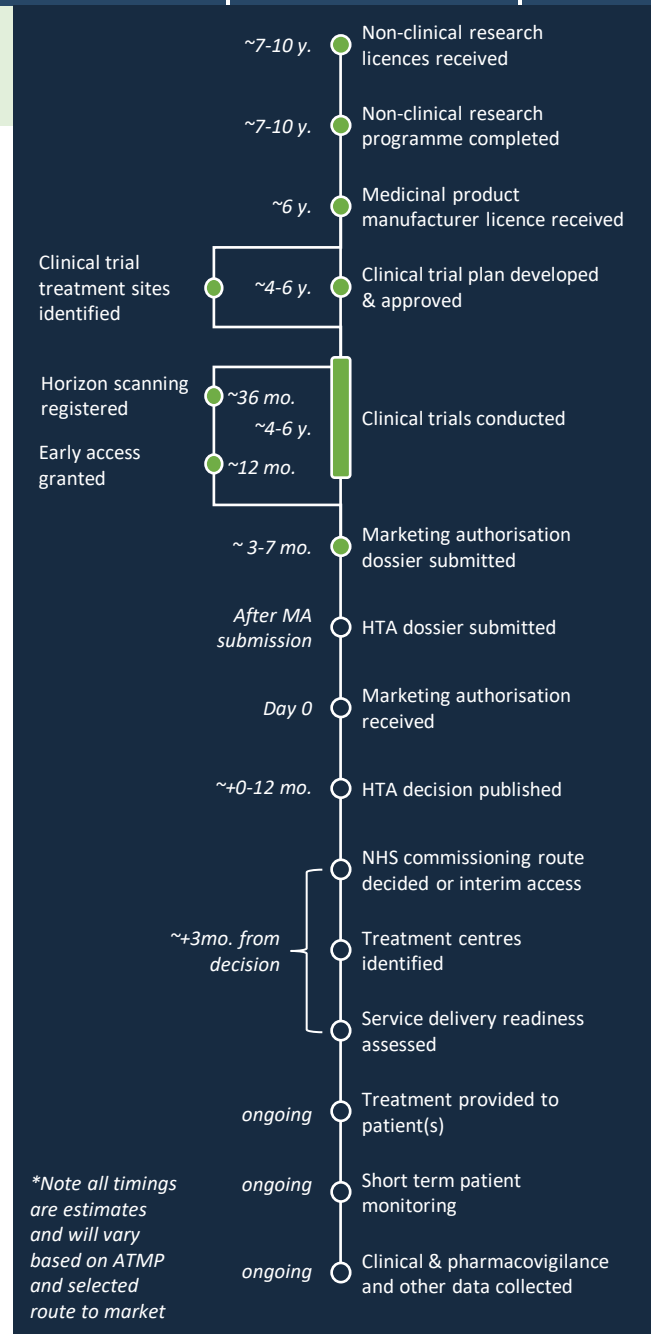
## KEY TOPICS

- Early advice on Market Access process [optional]
- **Health Technology Assessment Technology Appraisal**
- Health Technology Assessment Highly Specialised Technologies evaluation

Overview | To-do list | Output

- Be ready to provide clarifications at the committee meeting if required
- Developers can also request a commercial or clinical surgery with NHS England to facilitate further targeted discussions. Commercial surgeries are often used to discuss a complex PAS or commercial agreement, whereas clinical surgeries allow for interfacing with the specialised commissioning team

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

**Overview** | To-do list | Output

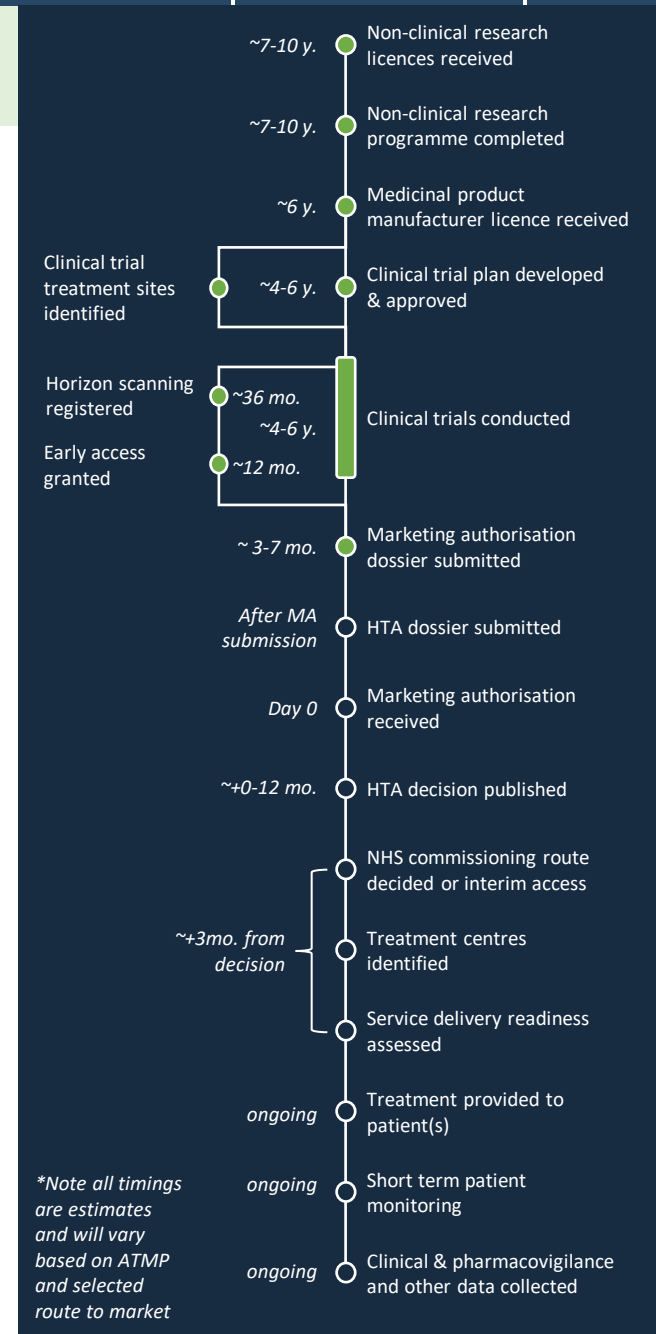
Prior to Developer submission, a number of activities will be completed by NICE:

- Provisional evaluation topics chosen (further detail on how NICE does this can be found here)
- NICE will identify that the ATMP should be submitted for highly specialised technology (HST) evaluation
- Scope preparation (this defines the disease, the patients eligible and the technologies covered by the appraisal and will include input from patient groups/PPI)
- Identification of consultees and commentators
- Briefing
- Referral of Evaluation topics

Once these steps are completed, developers should prepare and submit their evidence dossiers, which may include a commercial arrangement, along with a budget impact test assessment and attend an appraisal committee meeting with NICE stakeholders.

There are fees involved for the HTA process.





## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

Overview | **To-do list** | Output

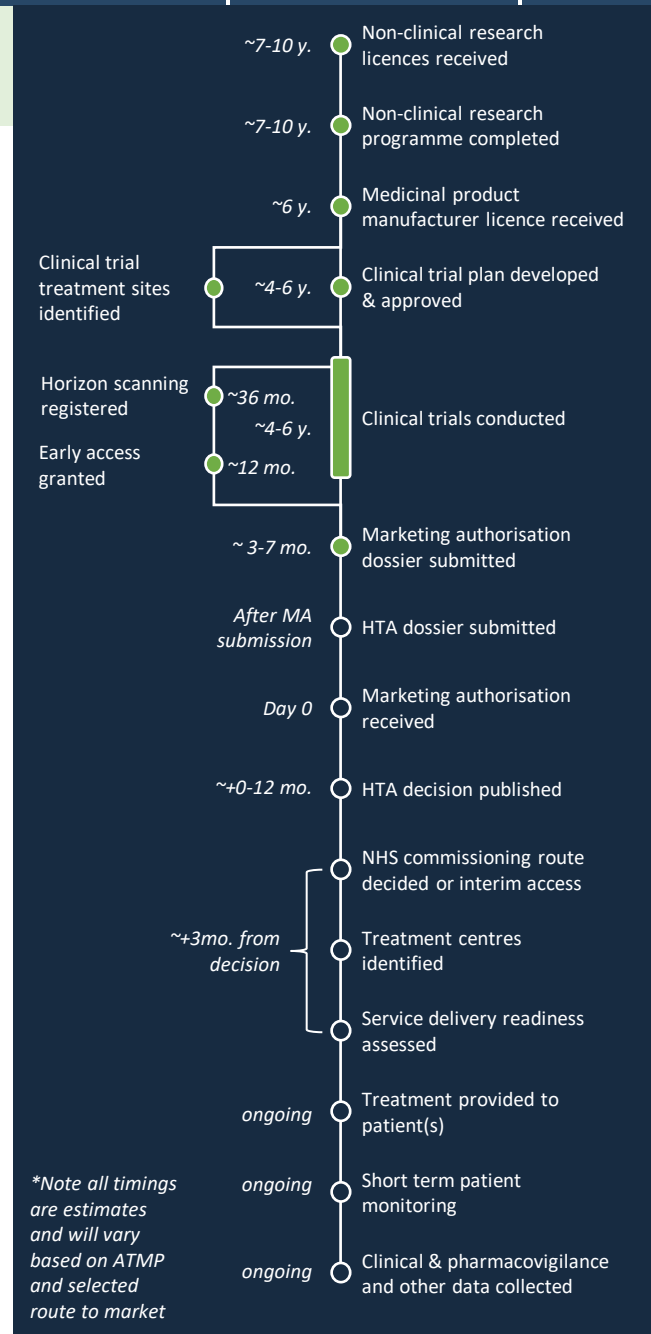
- Review NICE Highly Specialised Technology process and guidance here
  - Guidance from the ATTC on preparing for HTA for ATMPs can be found here
- Submit evidence to NICE along with (if required) commercial arrangement details using HST interim template which can be navigated to via the NICE guidance here
  - Refer to commercial arrangement topics below for details on requirements and approval
  - Guidance on economic modelling from EUNetHTA can be found here
  - Information on NICE's PRIMA service to healthcheck models used can be found here
- Complete budget impact assessment using NICE form here, further information can be found here
- Prepare for and attend Evaluation Committee meeting with NICE

**When**

- Developers should commence HTA process during MA application and aim for concurrent approvals of MHRA and NICE (subject to NICE capacity)

Note that NICE will not issue final guidance until MA has been received.

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

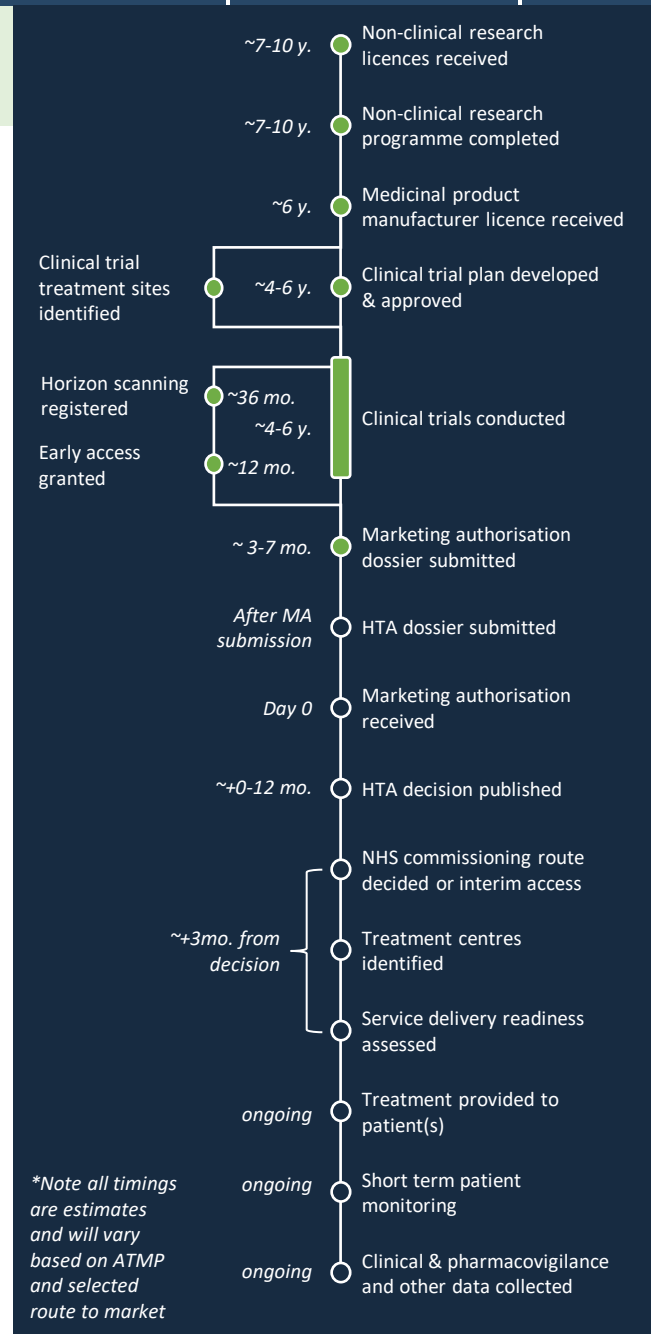


## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

Overview | To-do list | **Output**

- Evidence Review Group (ERG) assessment report
- Final evaluation determination (FED) following Evaluation committee and consultation
- NICE guidance issued with one of the following three recommendations:
  - Recommendation for routine commissioning
  - Recommendation for use with a Managed Access Agreement
  - Not recommended for routine commissioning




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

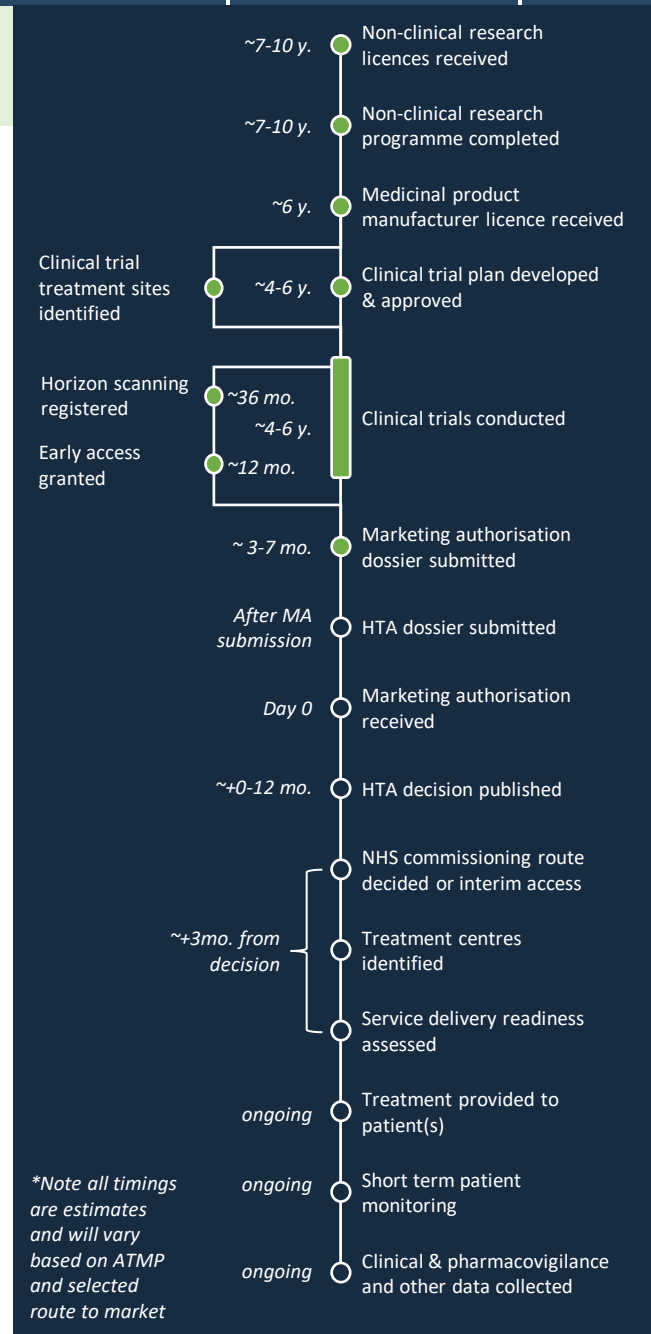
## Overview

## To-do list

- Horizon scanning registration
- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]
- Service delivery readiness

## Output

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

## Overview

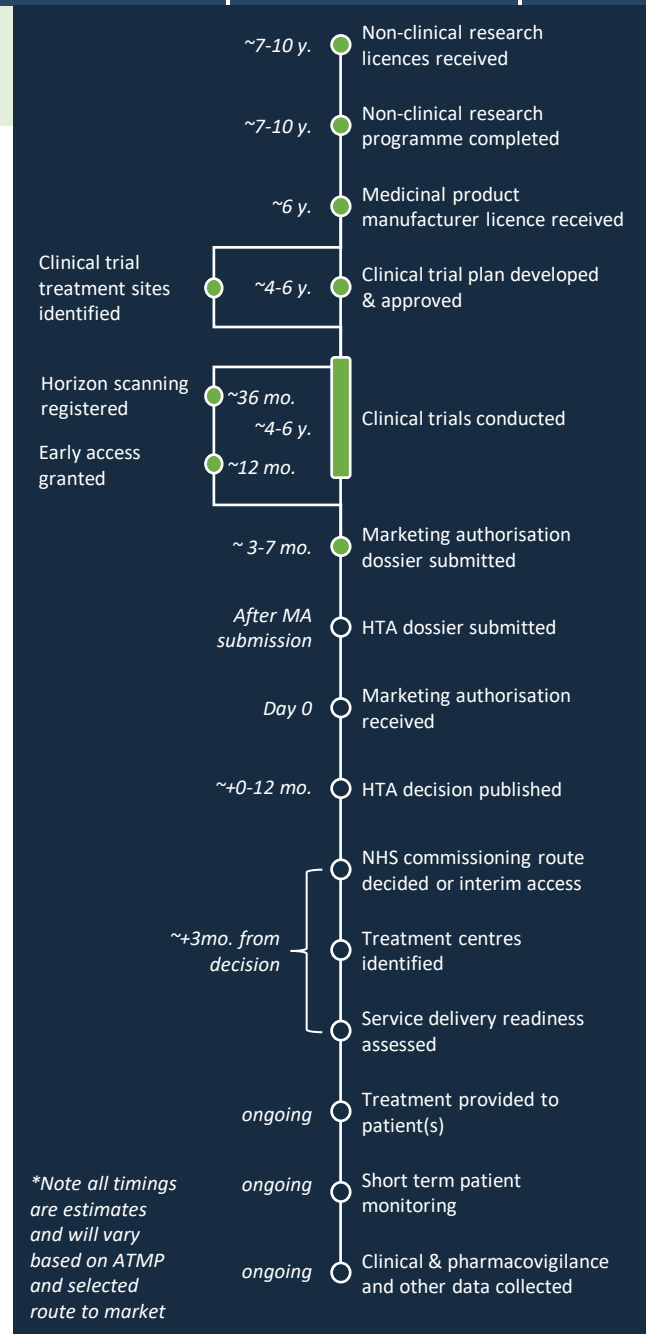
## To-do list

## Output

- ATMP developer
- NICE
- PPI
- NHSE

Linked steps | Who is involved? | Best practices & tips

**Variation by devolved nation**



## KEY TOPICS

- Early advice on Market Access process [optional]
- Health Technology Assessment Technology Appraisal
- **Health Technology Assessment Highly Specialised Technologies evaluation**

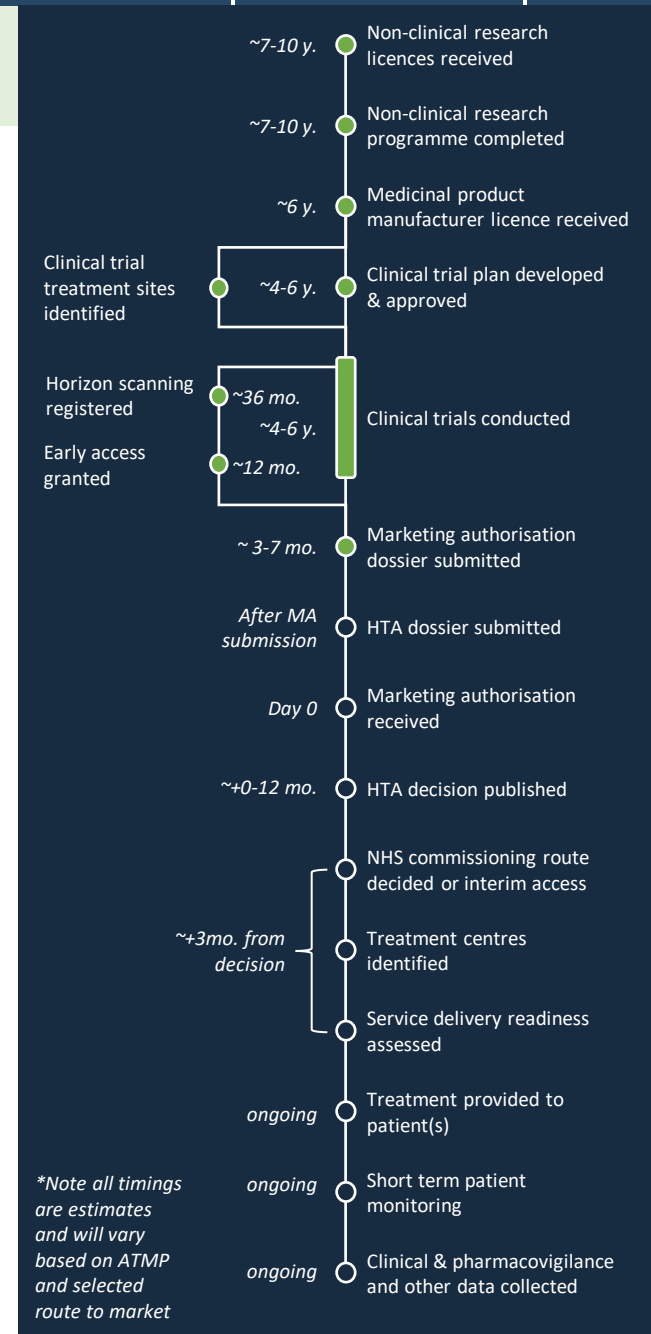
## Overview

## To-do list

## Output

- Developers should be prepared for ongoing engagement and additional informal meetings outside of the formal/prescribed process to assist with information exchange

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

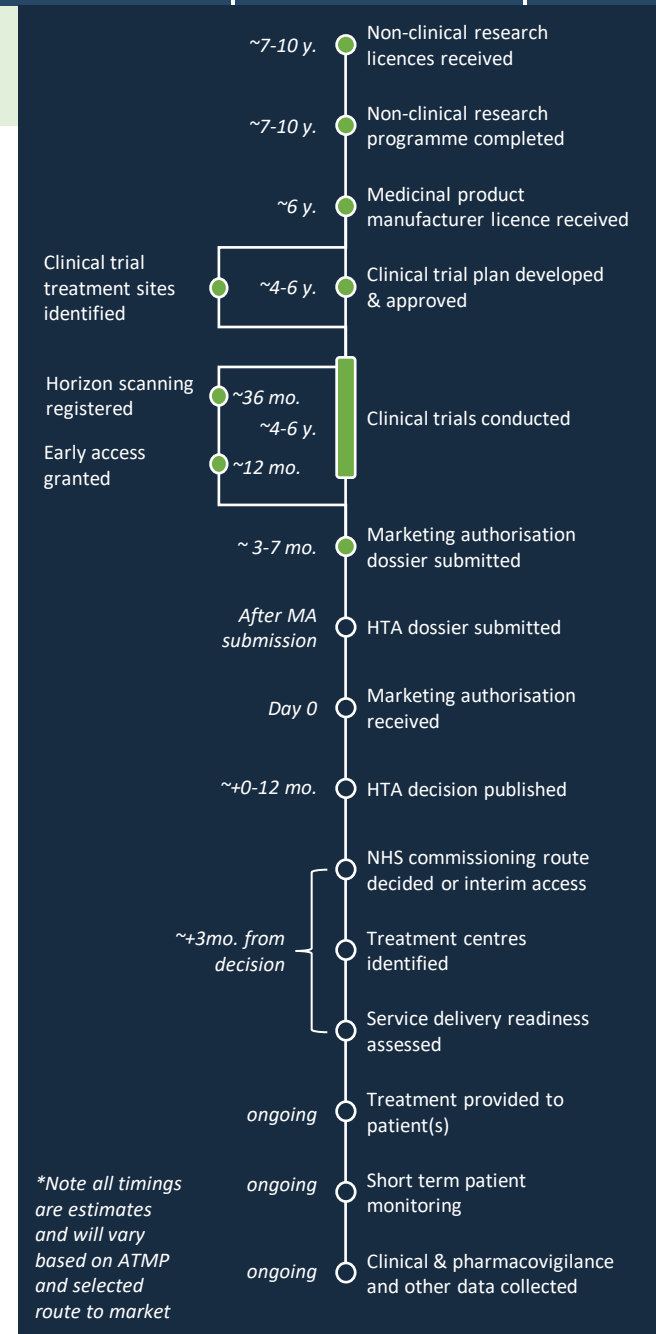
Overview | To-do list | Output

Appraisal of medicines by NICE (TA/HST) or AWMSG is the preferred route for making medicines available to patients in Wales. To avoid duplication, AWMSG would not usually appraise a medicine if NICE intends to appraise the same medicine for the same indication (see details of AWMSG's exclusion criteria here). There may be occasions where AWMSG requests a submission ahead of NICE guidance. In such circumstances, subsequent NICE guidance for the same medicine and indication supersedes AWMSG advice.

The All Wales Therapeutics and Toxicology Centre (AWTTC) will determine whether a medicine meets the criteria for appraisal by AWMSG after consideration of the initial submission (Form A) provided by the MA holder. The onus for engagement lies with the MA holder, although the AWTTC horizon scanning process also informs the AWMSG appraisal process and AWTTC may choose to refer a company to the appraisal process by requesting an initial submission.

**Next >**

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

Overview | To-do list | Output

The One Wales Medicines Process provides an alternative route to access a medicine in the interim period prior to NICE/AWMSG appraisal advice*, for clearly defined and specific cohorts of patients. There must, however, be a clearly identified unmet clinical need and a clear and binding commitment by the ATMP MA holder to collect appropriate patient outcome data and to engage in a future medicines appraisal by NICE or AWMSG. Suggestions for medicines to be considered via the One Wales Medicines Process can be made by Health Board Individual Patient Funding Request (IPFR) panels, Welsh Health Specialised Services (WHSSC), Chief Pharmacists, formulary pharmacists, Drugs & Therapeutics Committees or clinical experts (usually through their specialist group or network)**.

**< Previous**

*One Wales Interim decisions are interim to NICE guidance/AWMSG advice.
**Requests for medicines to be considered by the One Wales Medicines Process cannot be accepted from pharmaceutical companies



## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

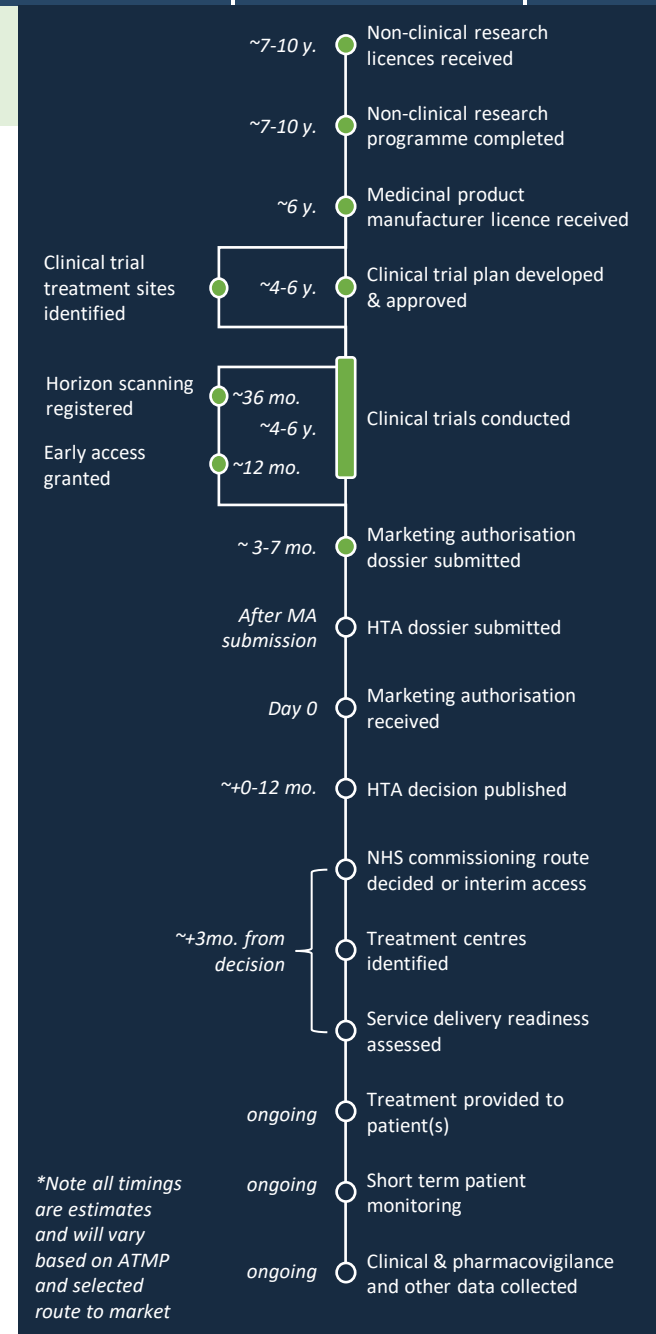
Overview | **To-do list** | Output

- Review AWMSG appraisal process guidance here and submit Form A
  - AWMSG/AWTTC document "Access to medicines for patients in Wales" can be accessed here
  - ABPI guidance on market access in Wales can be found here
  - Contact AWTTC via awttc@wales.nhs.uk to discuss any queries
- Share details of commercial agreements associated with NICE guidance (MAA, CAA, PAS) or equivalent with National Procurement Lead Pharmacist for Wales and Commercial Medicines Access Team (CMAT) via NHSWales.CA@wales.nhs.uk
  - To propose a Wales Patient Access Scheme review guidance from AWMSG here and submit here
- See information on how medicines are selected for the One Wales Medicines Process here

### When

- MA holders should engage with AWMSG with regard to appraisal of their medicine as early as possible and before MA is received. Note that AWMSG will not issue advice until MA has been received
- If applicable, MA holders should get in touch with the National Procurement Lead Pharmacist for Wales with regard to commercial agreements as early as possible and before NICE guidance is published.

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



**KEY TOPICS**

**AWMSG Medicines Appraisal and One Wales Medicines Process**

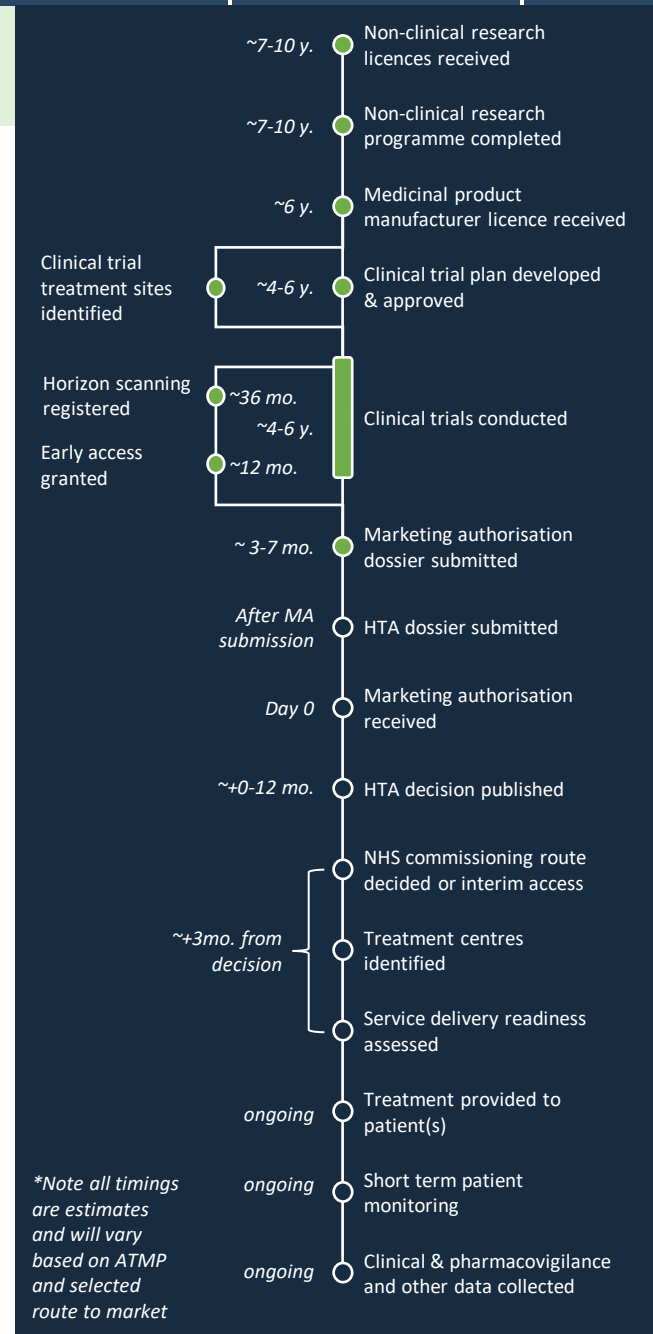
Overview | To-do list | **Output**

- NHS Wales implementation of NICE guidance (TA/HST)***
- Where NICE guidance is associated with a commercial agreement, implementation in NHS Wales is subject to the medicine being made available in Wales via a commercial agreement which offers equivalent value to the agreement available in England
- AWMSG advice
  - AWMSG Secretariat Assessment Report (ASAR)
  - Final Appraisal Recommendation following AWMSG meeting, subsequently ratified by Welsh Government

**Next >**

*** In line with Welsh Government statutory requirements, health boards and trusts in Wales are required to make medicines recommended by NICE or AWMSG available within 60 days (60 days from FAD/FED or Welsh Government ratification, respectively)





**KEY TOPICS**

**AWMSG Medicines Appraisal and One Wales Medicines Process**

Overview | To-do list | **Output**

- AWMSG recommendations options are as follows:
  - Recommended for use within NHS Wales (for first in class medicines)
    - Funding may be provided via the New Medicines Fund †
  - Recommended as an option for use within NHS Wales (for later entrants i.e. second, third, etc. in class medicines)
  - Recommended for restricted use within NHS Wales/ Recommended as an option for restricted use within NHS Wales
    - Applies when use of the medicine is approved for a specific section of the licensed indication or a specific patient population (restriction/s will be detailed within the final recommendation)
  - Not recommended for use
- If applicable, One Wales Interim decision

Note all products recommended for use by AWMSG and NICE must be made available through the standard commissioning process

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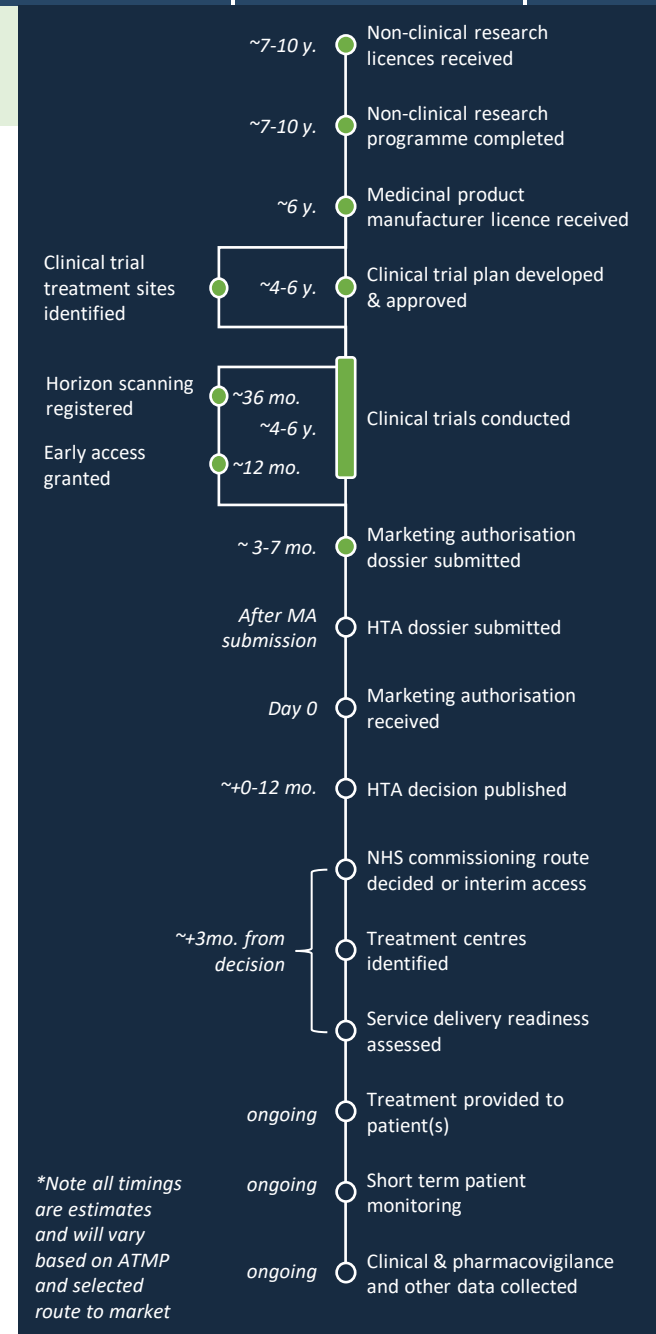
† Medicines that are funded via the New Medicines Fund are also required to be made available within 60 days (60 days from FAD/FED or Welsh Government ratification, respectively)





## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

## Overview

## To-do list

## Output

Patient Access Scheme [optional]

Service delivery readiness

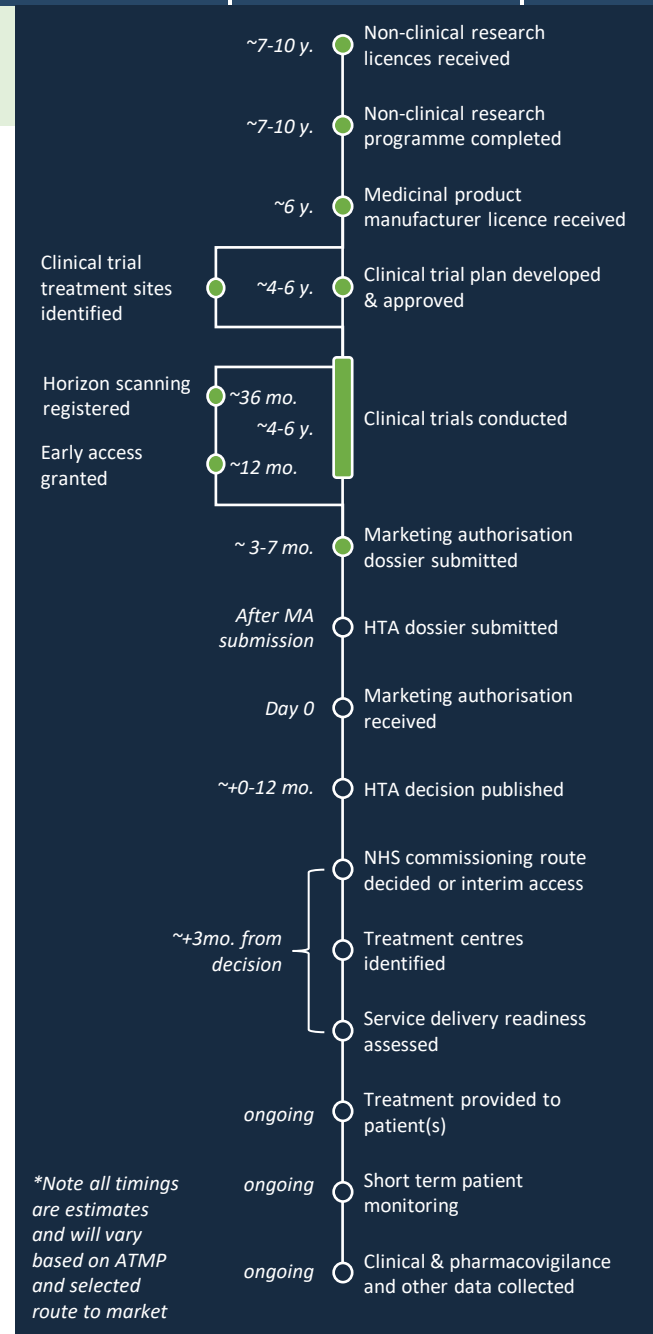
Linked steps

Who is involved?

Best practices & tips

Back to England TA

Back to England HST



1 What programmes are available to accelerate time to market?

2 How can an ATMP obtain early access through EAMS?

3 What are the routes for ATMP reimbursement assessment?

4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

## Overview

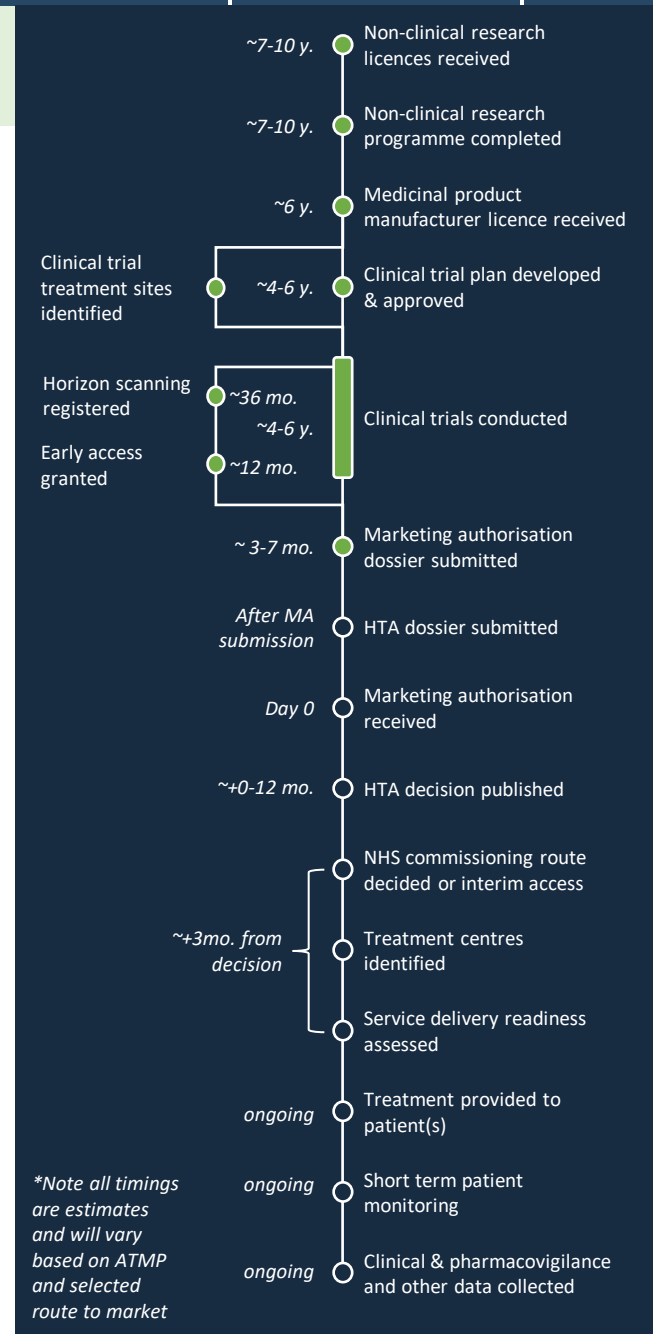
## To-do list

## Output

- AWMSG
- AWTTC
- One Wales Medicines Assessment Group (OWMAG)
- ATMP MA holder (developer)

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Back to England TA** | **Back to England HST**



## KEY TOPICS

**AWMSG Medicines Appraisal and One Wales Medicines Process**

Overview | To-do list | Output

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST

## KEY TOPICS

- **SMC Health Technology Assessment Technology Appraisal submission**
- SMC Health Technology Assessment Ultra-Orphan submission

**Overview** | To-do list | Output

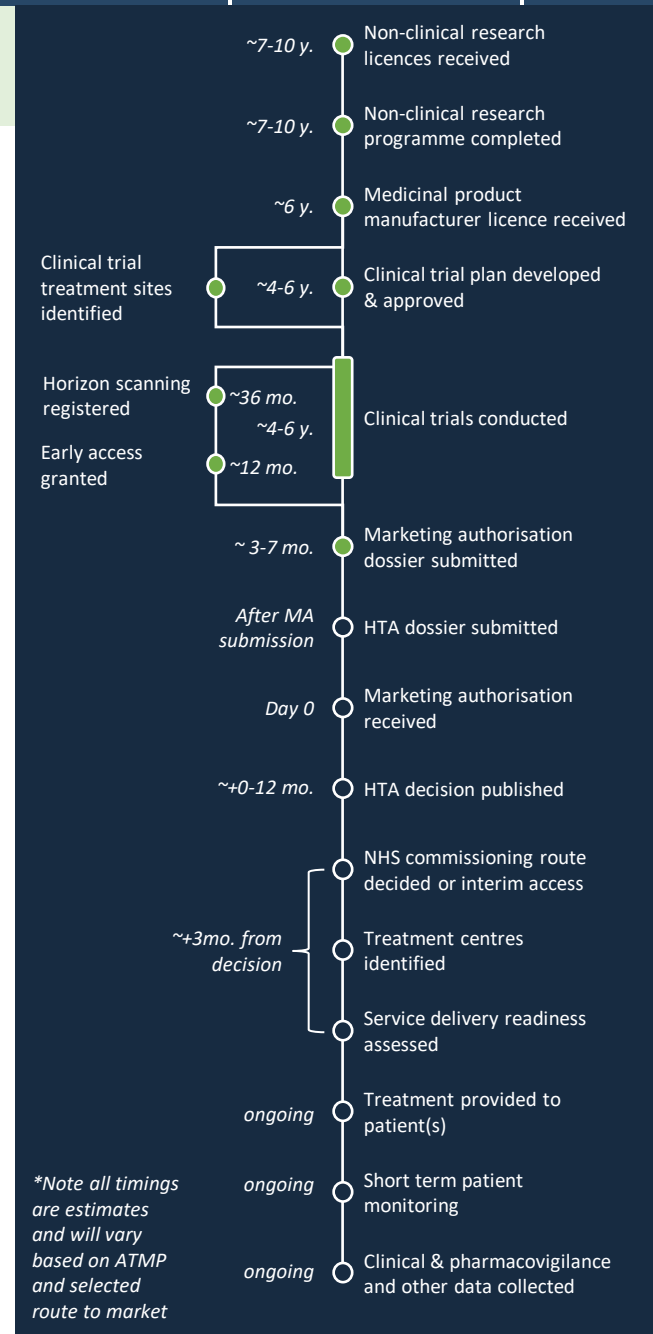
To provide a medicine in Scotland, developers are required to make a submission to the SMC for Health Technology Assessment. Their evidence submission will be assessed by the SMC team of pharmacists, health service researchers and economists (PASAG assess the PAS submission in parallel).

SMC's New Drugs Committee (NDC) will meet to evaluate evidence and make a "yes/no" recommendation to the SMC. If the NDC recommendation is positive, the medicine will go to the SMC Executive for review and final decision, and the final Decision Advice Document (DAD) is published, as per SMC timelines.

If NDC recommendation is negative, the developer can request a Patient and Clinician Engagement (PACE) meeting to be held, if their medicine is eligible for PACE. The developer will be able to comment on the NDC assessment and recommendation and, if required, submit relevant (re)analyses and/or an updated PAS application. The SMC committee meeting will then consider the NDC recommendation, in light of the Company Comments to the DAD, Patient Group submissions and PACE outcomes, and apply relevant modifiers before making the final decision. The DAD is then published and distributed to health boards.

Note: for second or third in class medicines (including ATMPs), developers can elect to go through the abbreviated route, if their medicine qualifies for this route.

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

**SMC Health Technology Assessment Technology Appraisal submission**

SMC Health Technology Assessment Ultra-Orphan submission

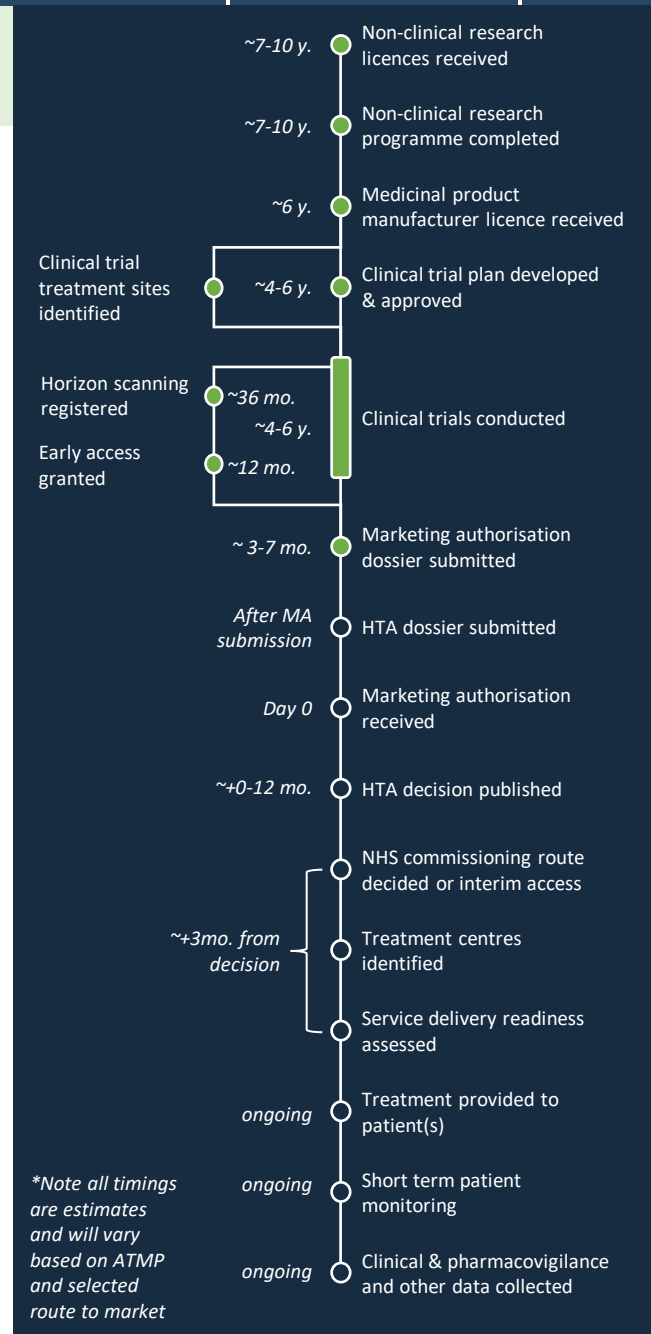
Overview | **To-do list** | Output

- Contact the SMC about an intended submission here
- Submit New Product Assessment Form (NPAF) to SMC for assessment
  - NPAF form can be found here
  - Guidance on the NPAF can be found here
- Developers will be invited to comment on NDC DAD
  - Submit relevant (re)analyses and/or PAS submission (if required)
  - Submit PACE statement (if requested)
    - Further guidance and resources on the PACE process can be found here
- Guidance on the abbreviated SMC assessment route can be found here
  - The abbreviated submission template can be found here

**When**

SMC aims to publish advice at the time of or soon after Marketing Authorisation, Manufacturers should liaise closely with SMC regarding submission plans and timings





## KEY TOPICS

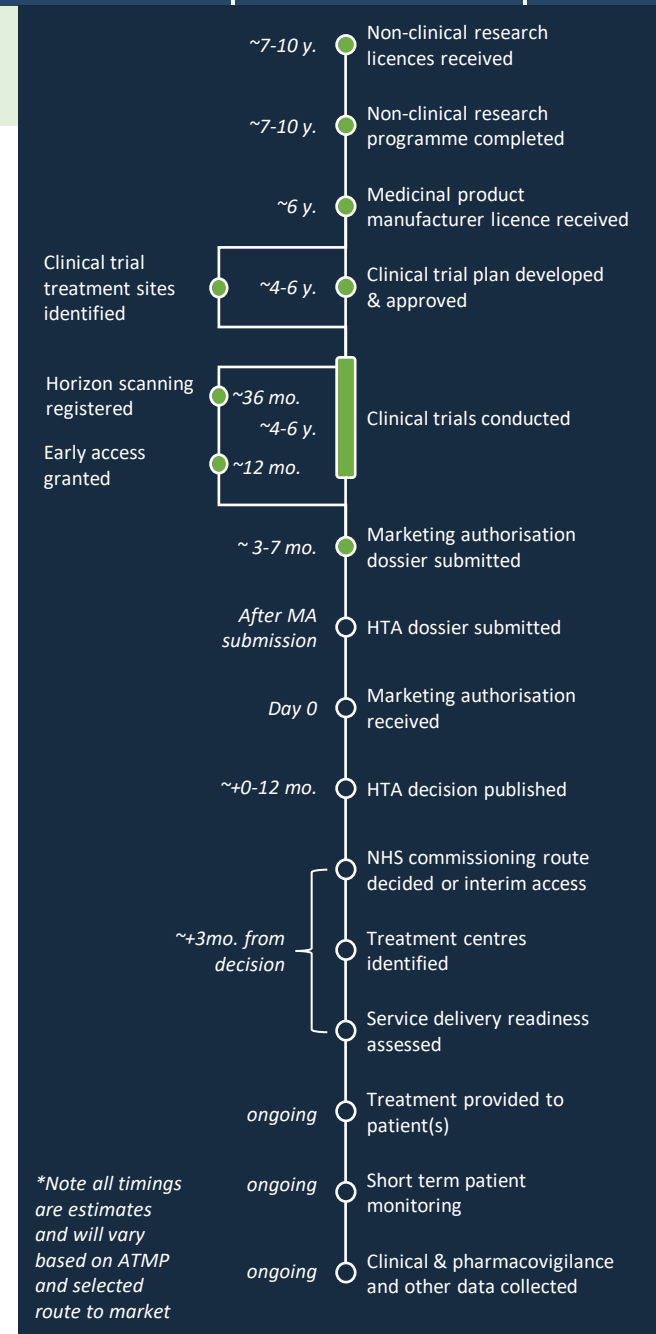
**SMC Health Technology Assessment Technology Appraisal submission**

SMC Health Technology Assessment Ultra-Orphan submission

Overview | To-do list | **Output**

- SMC decision and publication of DAD
- Medicine accepted for routine use in line with licence
- Medicine accepted with some restriction relative to licence
- Medicine accepted on interim basis subject to ongoing evaluation and reassessment
  - NHS boards required to consider SMC accepted advice and make the medicine, or an equivalent SMC accepted medicine available
- Medicine not recommended for use
  - Requests for individual patients to be treated with medicine can be considered via the Peer Approved Clinical System (PACS) tier 2

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

**SMC Health Technology Assessment Technology Appraisal submission**

SMC Health Technology Assessment Ultra-Orphan submission

## Overview

## To-do list

## Output

Patient Access Scheme [optional]

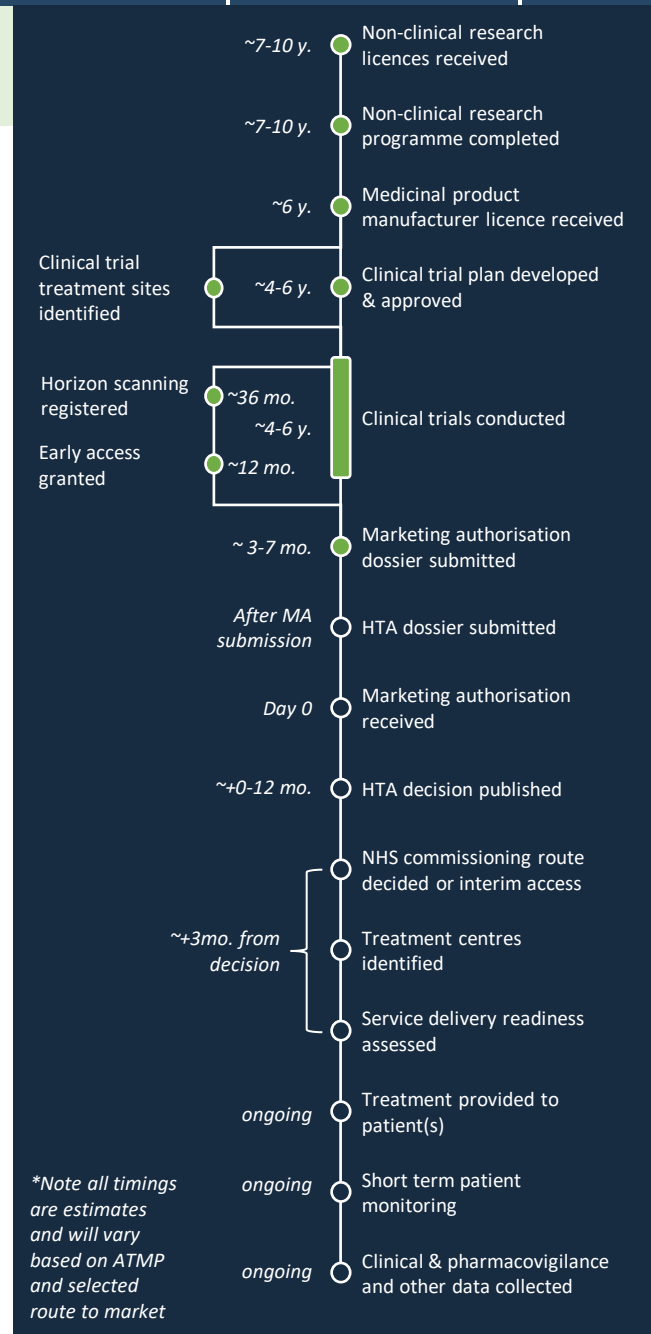
Linked steps

Who is involved?

Best practices & tips

Back to England TA

Back to England HST



## KEY TOPICS

**SMC Health Technology Assessment Technology Appraisal submission**

SMC Health Technology Assessment Ultra-Orphan submission

## Overview

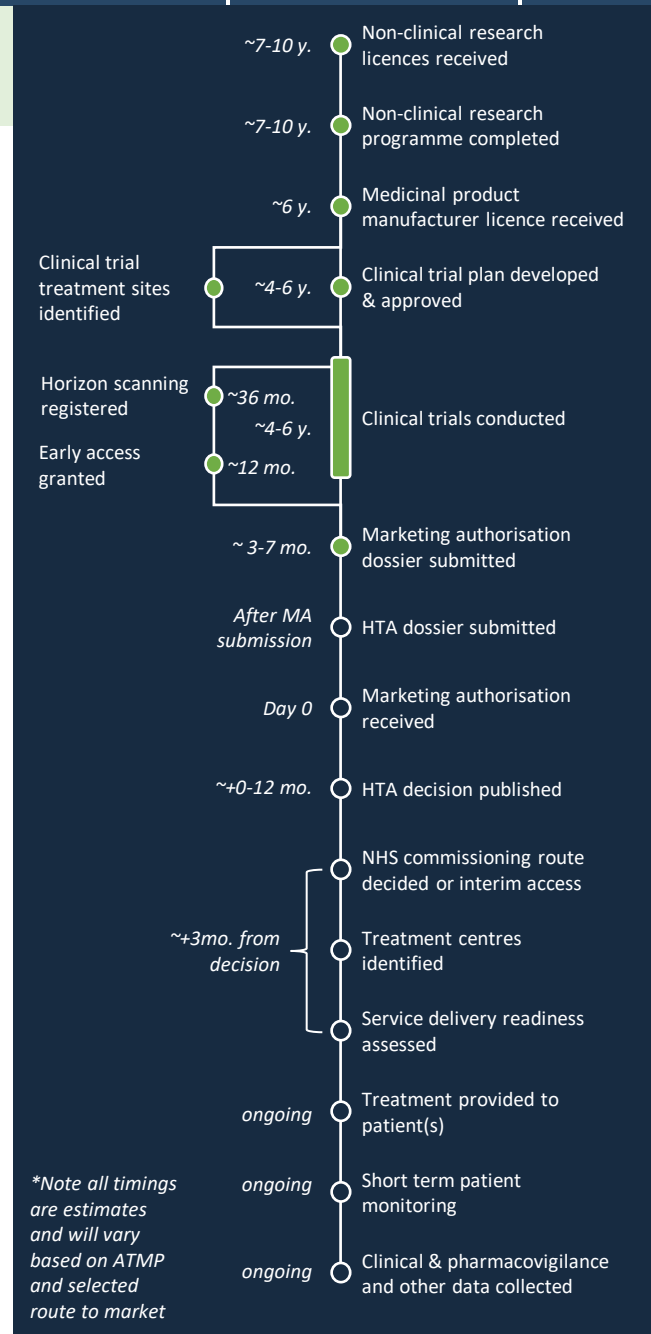
## To-do list

## Output

- SMC
- ATMP developer

Linked steps | Who is involved? | Best practices & tips

Back to England TA | Back to England HST



1 What programmes are available to accelerate time to market?

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3 What are the routes for ATMP reimbursement assessment?

4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

**SMC Health Technology Assessment Technology Appraisal submission**

SMC Health Technology Assessment Ultra-Orphan submission

## Overview

## To-do list

## Output

Linked steps

Who is involved?

Best practices & tips

Back to England TA

Back to England HST

## KEY TOPICS

SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

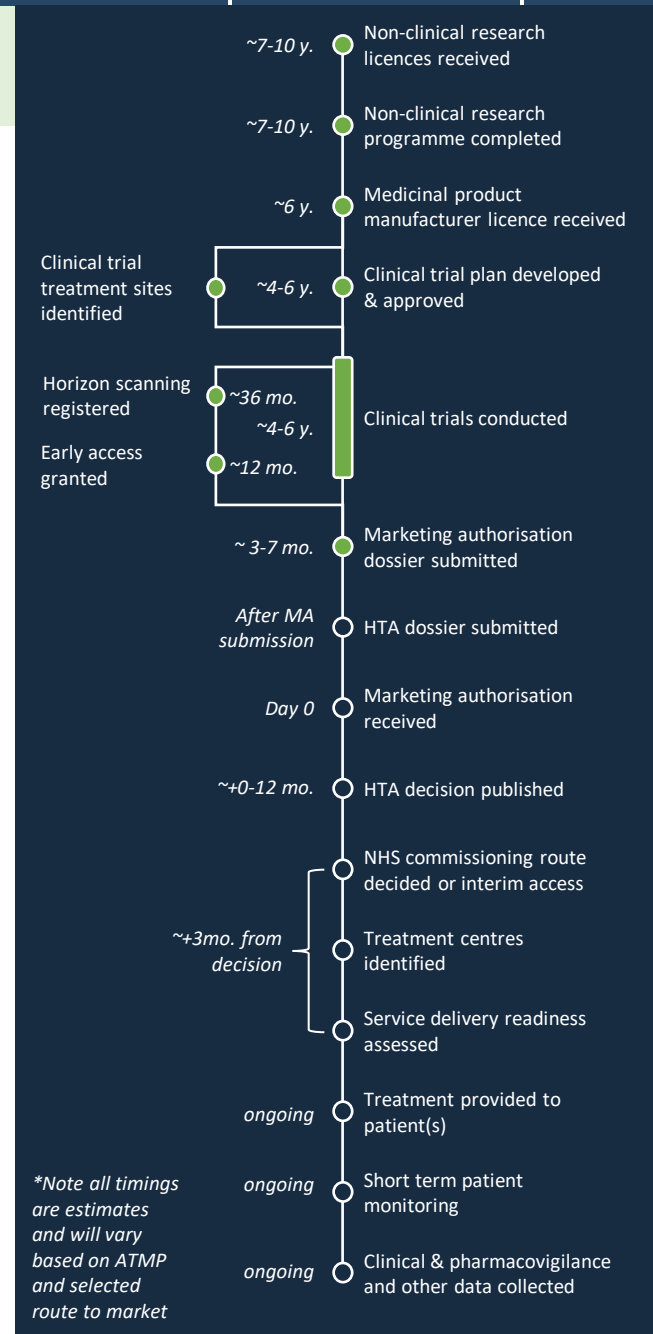
**Overview** | To-do list | Output

Developers should identify whether the standard TA submission route or the ultra-orphan HTA route applies to their product. If a developer believes that their product meets the criteria for ultra-orphan, manufacturers must first submit for validation as an ultra- orphan medicine by the SMC. If validated, manufacturers then submit a New Product Assessment Form (NPAF) for Ultra-Orphan Medicines, for initial SMC assessment.

A Patient Access Scheme is mandatory as part of this submission. During the initial assessment phase, developers must create a data collection plan, which must be submitted to Scottish Government prior to the product being made available in Scotland. Following initial SMC assessment, the product will become available on the NHS for up to three years while the company generates further evidence on its effectiveness.

At three years, or before, the developer submits a revised NPAF, for SMC to reassess the evidence and make their decision on its routine use in NHS Scotland. For all ultra-orphan reassessments, a PACE meeting will be held and a revised PAS offered, if required.

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

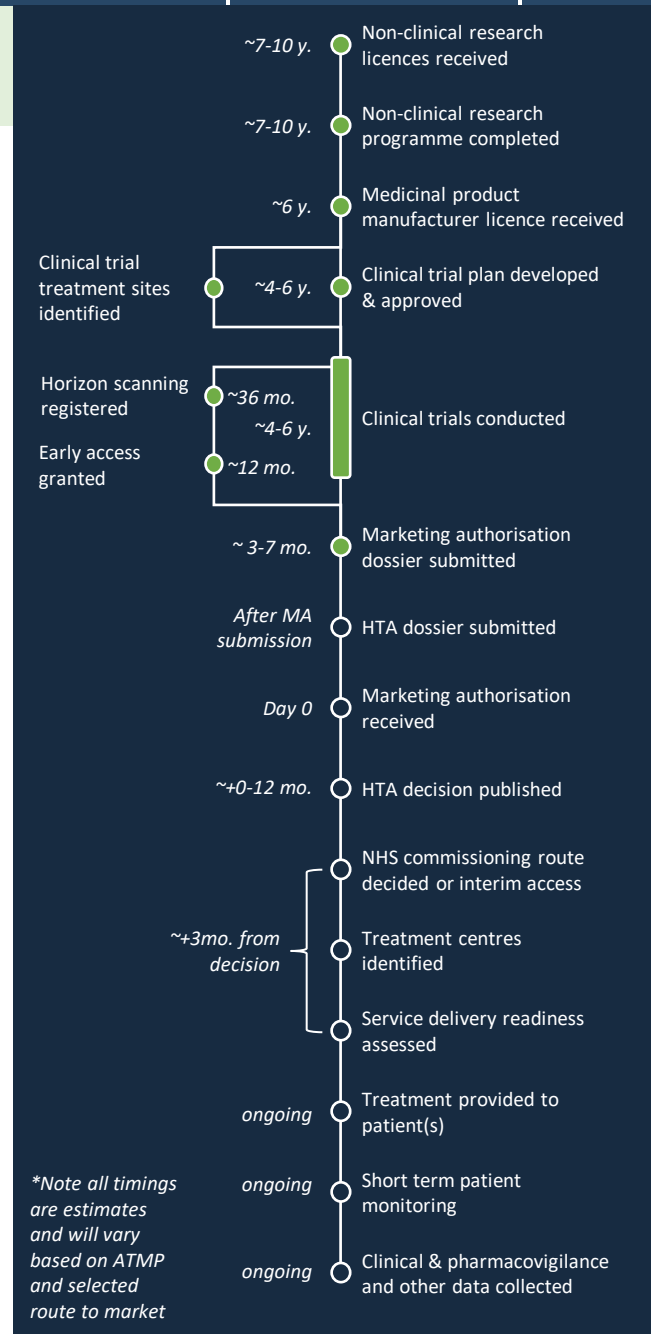
Overview | **To-do list** | Output

- Developers should review the SMC guidance on eligibility and process for the ultra-orphan pathway here
- Submit the ultra-orphan proforma to SMC for validation here
- Submit the New Product Assessment Form (NPAF) for Ultra-Orphan Medicines for initial SMC assessment
  - Ultra-orphan NPAF can be found here
  - Include PAS in submission (refer to PAS topic)
- Develop data collection plan and submit to the Scottish government here
- Provide full submission following period of data collection for SMC re-assessment
  - Submit new PAS submission (if required)
  - Submit PACE statement (if requested)
    - Further guidance and resources on the PACE process can be found here

**When**

- Submit for validation assessment at an early stage, prior to Marketing Authorisation
- SMC aims to publish advice at the time of or soon after Marketing Authorisation, Manufacturers should liaise closely with SMC regarding submission plans and timings
- Submit the data collection plan to Scottish Government within 3 months of receiving the SMC initial assessment report

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

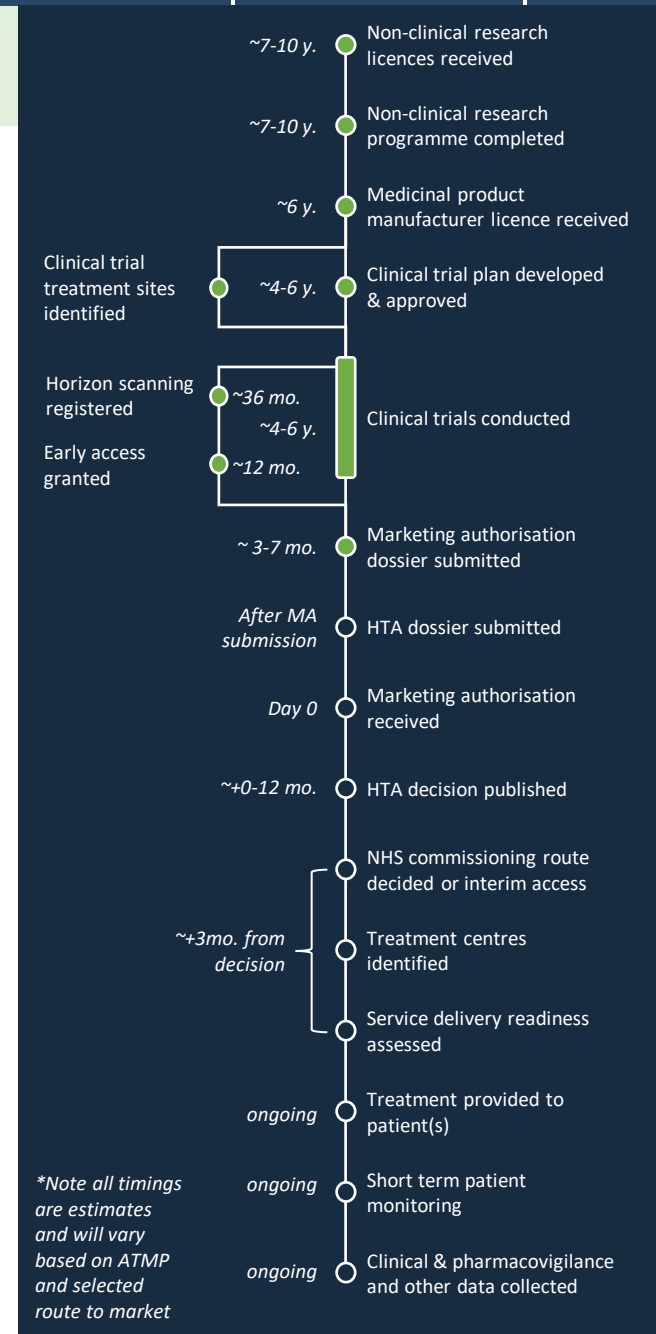
SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

Overview | To-do list | **Output**

- SMC initial assessment report
- Manufacturer developed data collection plan
- Medicine available for use in Scotland, during agreed period of data collection
  - Funding available from Ultra-Orphan Drug Risk Share Scheme (pools funds from all Health Boards)
- Subsequent SMC assessment report
- Medicine accepted for routine use in line with licence or
- Medicine accepted with some restriction relative to licence
  - NHS boards required to consider advice and make the medicine, or an equivalent SMC accepted medicine available
  - Funding available from Health Board budget and/or New Medicines Fund (to confirm NMF use)
- Medicine not recommended for use
  - Requests for individual patients to be treated with medicine can be considered via the Peer Approved Clinical System (PACS) tier 1

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



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## KEY TOPICS

SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

## Overview

## To-do list

## Output

Patient Access Scheme

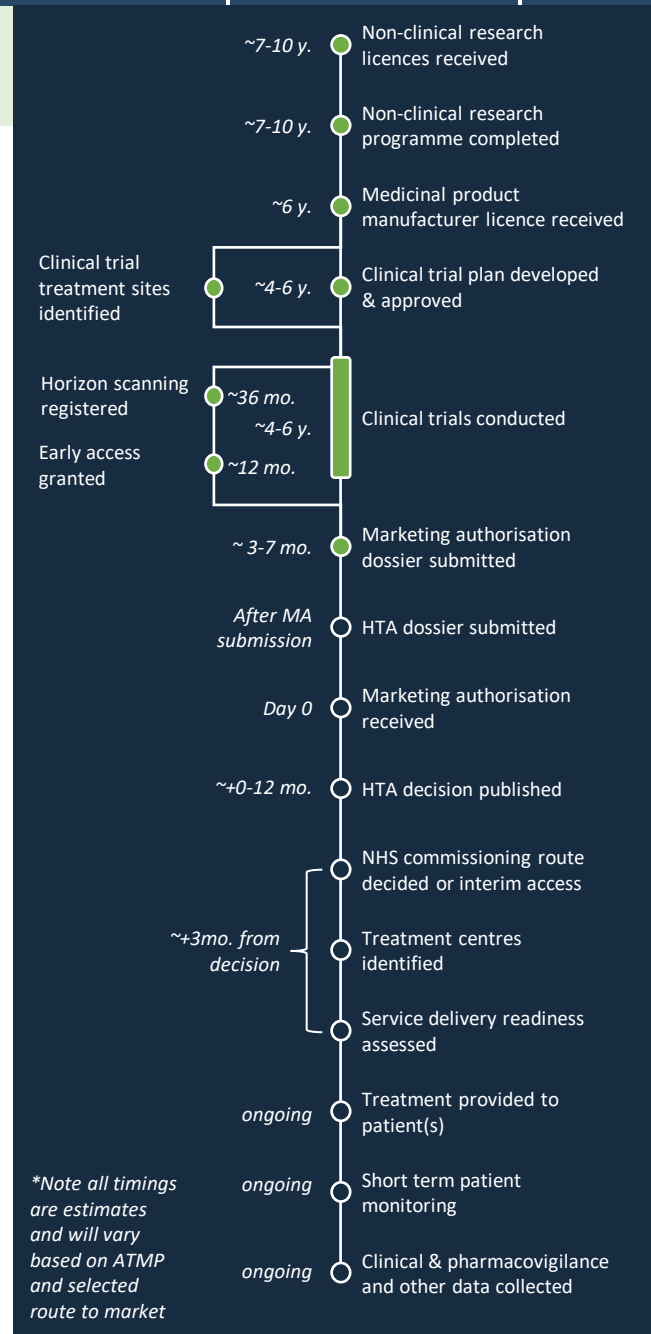
Linked steps

Who is involved?

Best practices & tips

Back to England TA

Back to England HST



## KEY TOPICS

SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

## Overview

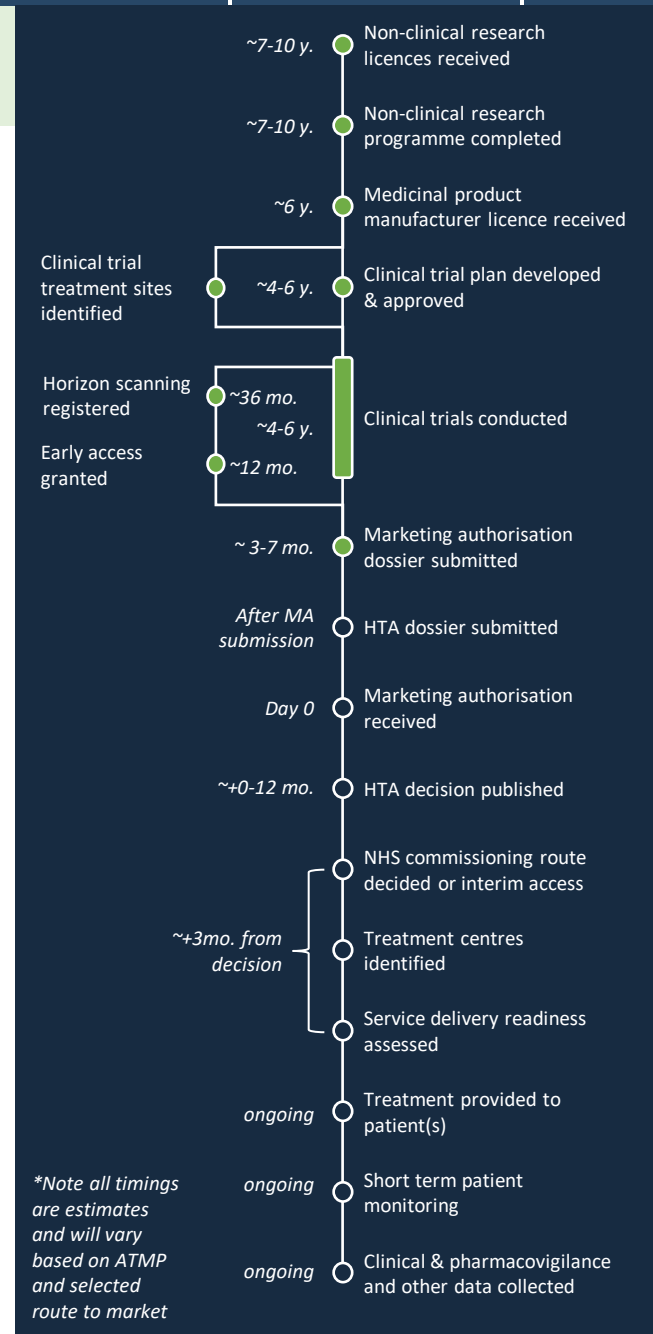
## To-do list

## Output

- SMC
- ATMP developer
- PASAG

Linked steps | Who is involved? | Best practices & tips

Back to England TA | Back to England HST



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## KEY TOPICS

SMC Health Technology Assessment Technology Appraisal submission

**SMC Health Technology Assessment Ultra-Orphan submission**

## Overview

## To-do list

## Output

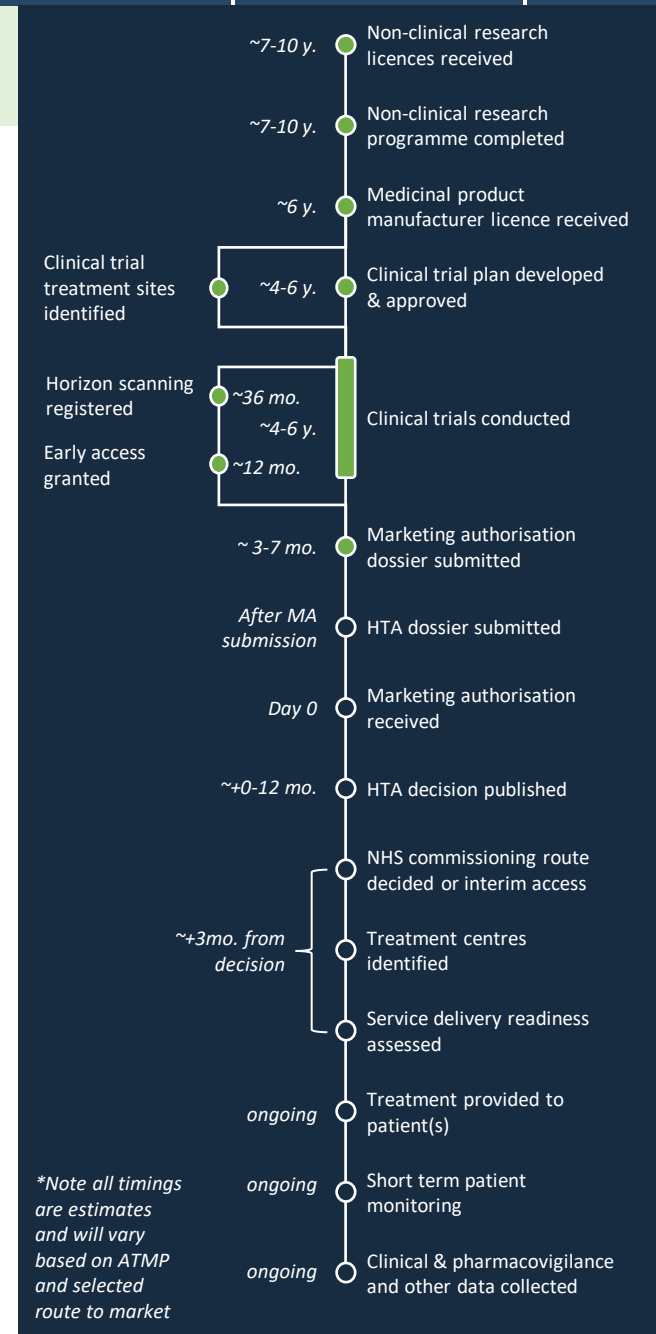
**Linked steps**

**Who is involved?**

**Best practices & tips**

**Back to England TA**

**Back to England HST**



## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

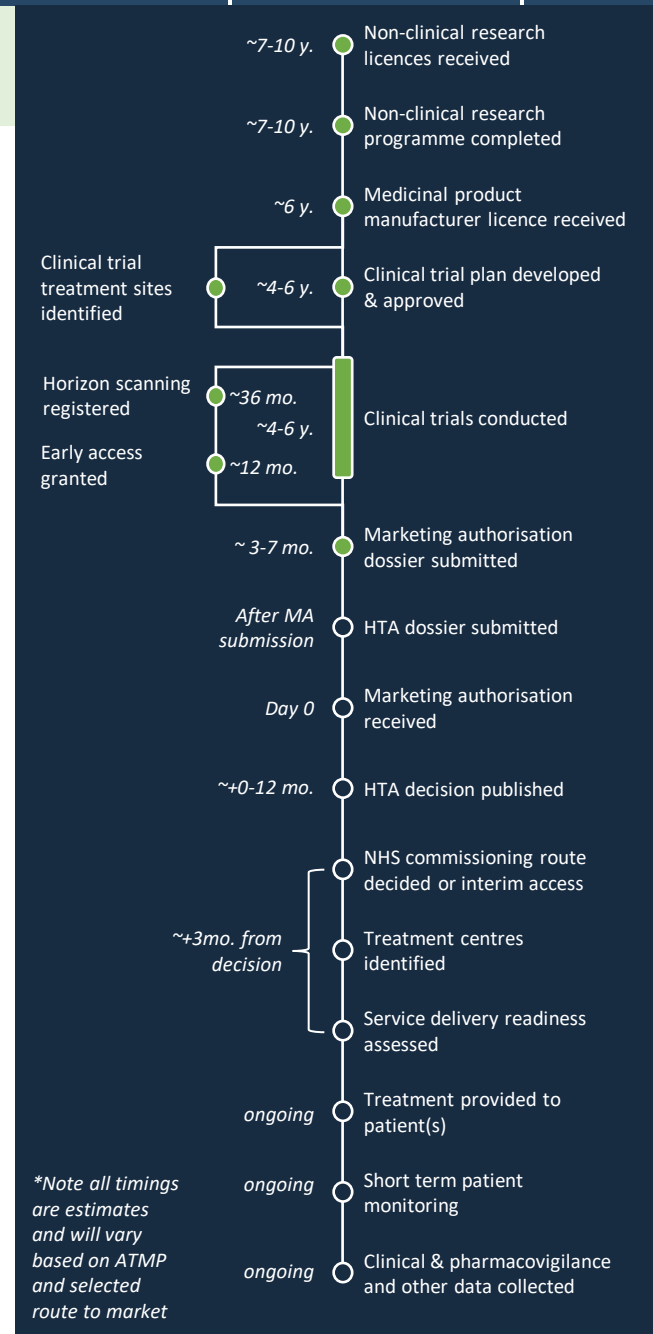
**Overview** | To-do list | Output

In Northern Ireland, there is no equivalent to England's National Institute of Health and Care Excellence (NICE). Instead, the Department of Health has a formal link with NICE whereby Technical Appraisal guidance published by the Institute is reviewed locally reviewed for applicability to Northern Ireland and, where appropriate, endorsed for implementation in Health and Social Care (HSC). As a result, the guidance may be endorsed with caveats to advise local HSC organisations of any changes necessary to align with equivalent legislation/policy or any specific instructions/requirements to adapt to NI circumstances.

Where NICE recommends new drugs for use within the Cancer Drugs Fund in England, these drugs will be made available in the same way as those drugs which have been recommended by NICE as suitable for routine commissioning. They will be prescribed by hospital clinicians in line with clinical guidelines and evidence.

Where NICE does not recommend a drug or appraisal has yet to take place (but drug is licenced), HSCB will consider Individual Funding Requests (IFR) made by clinicians to the Regional Scrutiny Committee on the grounds of clinical exceptionality defined here.

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST



## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

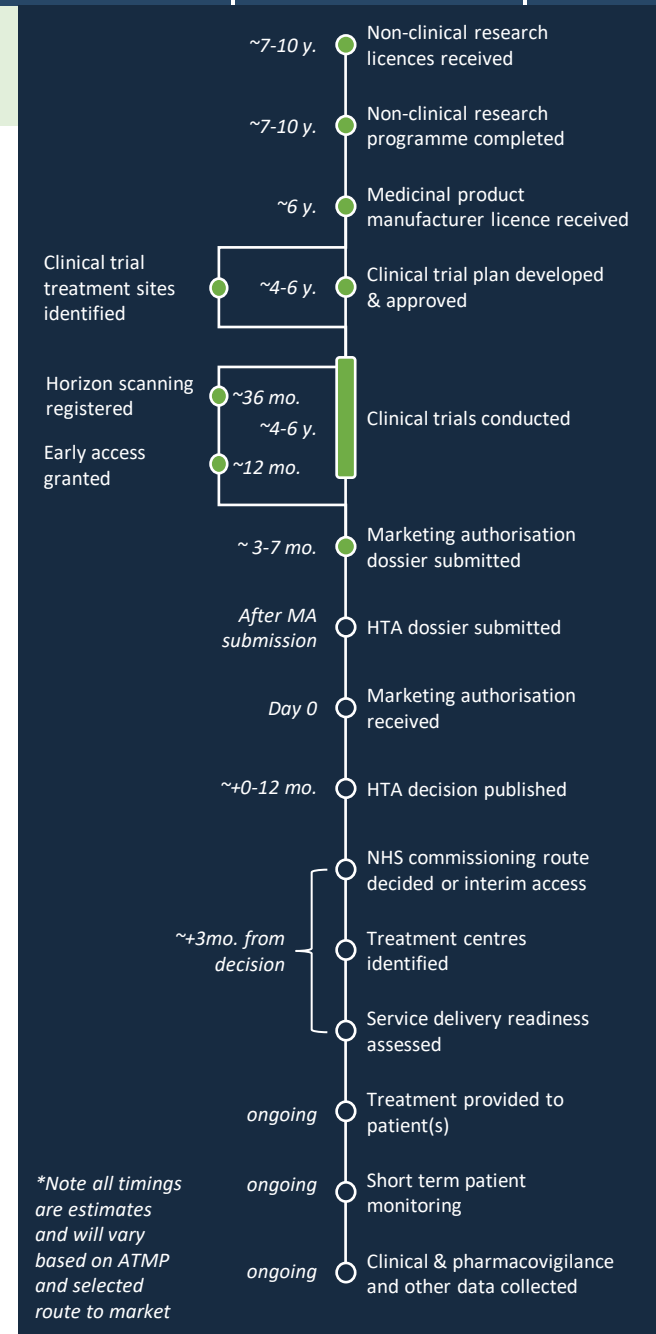
Overview | **To-do list** | Output

- Review NICE Technology Appraisal process and guidance here
- Submit evidence to NICE along with (if required) commercial arrangement details using TA submission template

**When**

- Developers should commence HTA process during MA application and aim for concurrent approvals of MHRA and NICE
- Note that NICE will not issue final guidance until MA has been received





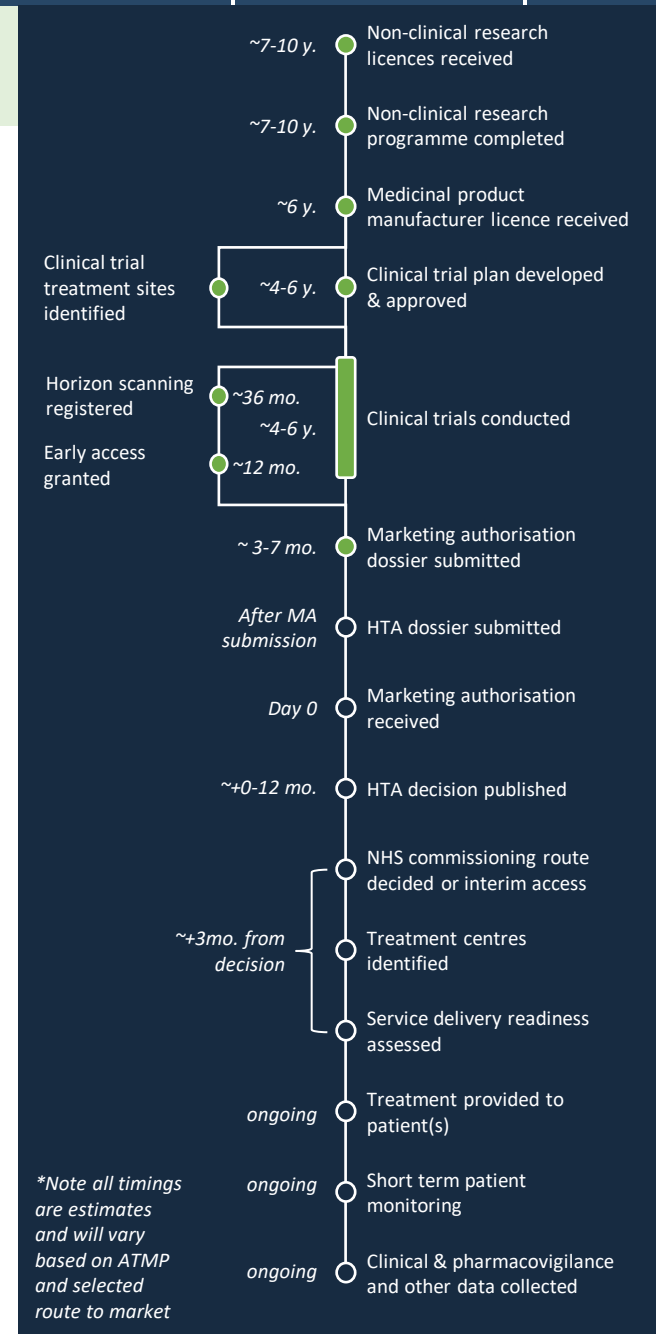
## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

Overview | To-do list | **Output**

- Evidence Review Group (ERG) assessment report
- Final appraisal document (FAD) following Appraisal committee and consultation
- NICE guidance issued with one of the following three recommendations:
  - Recommendation for routine commissioning
  - Recommendation for use with a Managed Access Agreement via CDF/IMF
  - Not recommended for routine commissioning
- For recommended Technology Appraisals that have been endorsed by Department of Health, service notifications are published on HSCB website outlining requirements for implication in Northern Ireland and commissioning arrangements
- For technology appraisals which have not been approved by NICE or endorsed by DHSC are referred to as “not recommended”





## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

## Overview

Health Technology Assessment Technology Appraisal

Patient Access Scheme [optional]

## To-do list

## Output

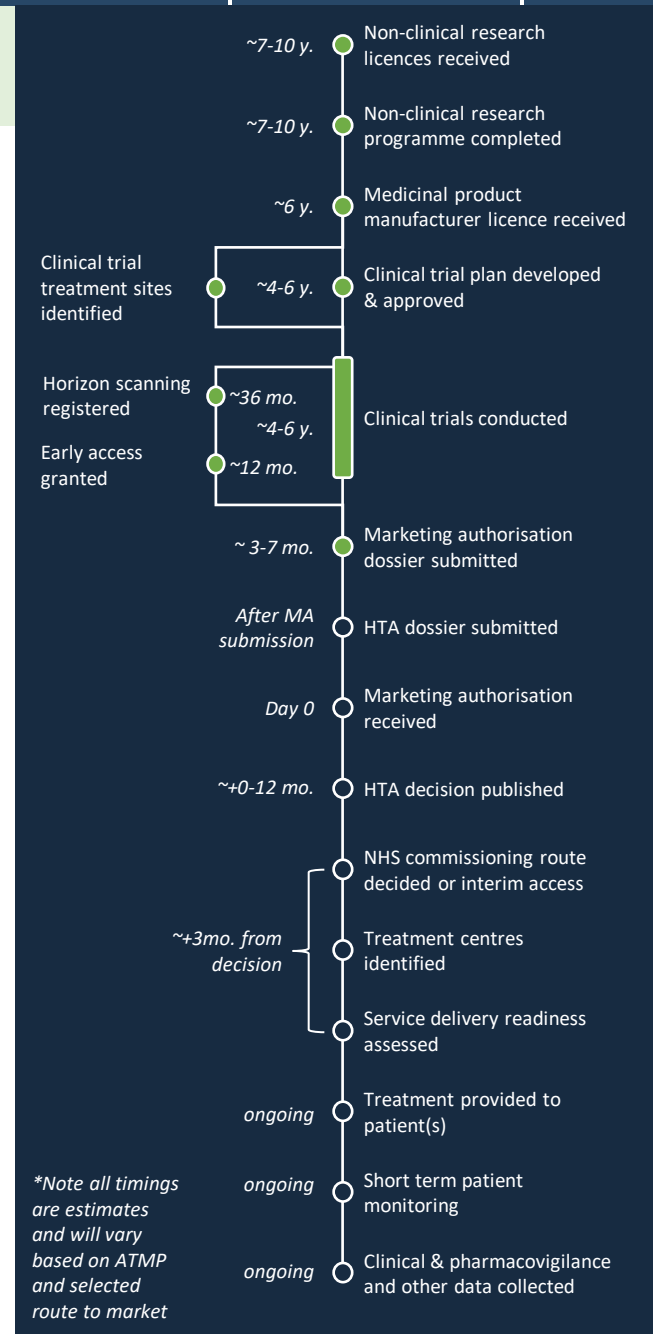
Linked steps

Who is involved?

Best practices & tips

Back to England TA

Back to England HST



## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

## Overview

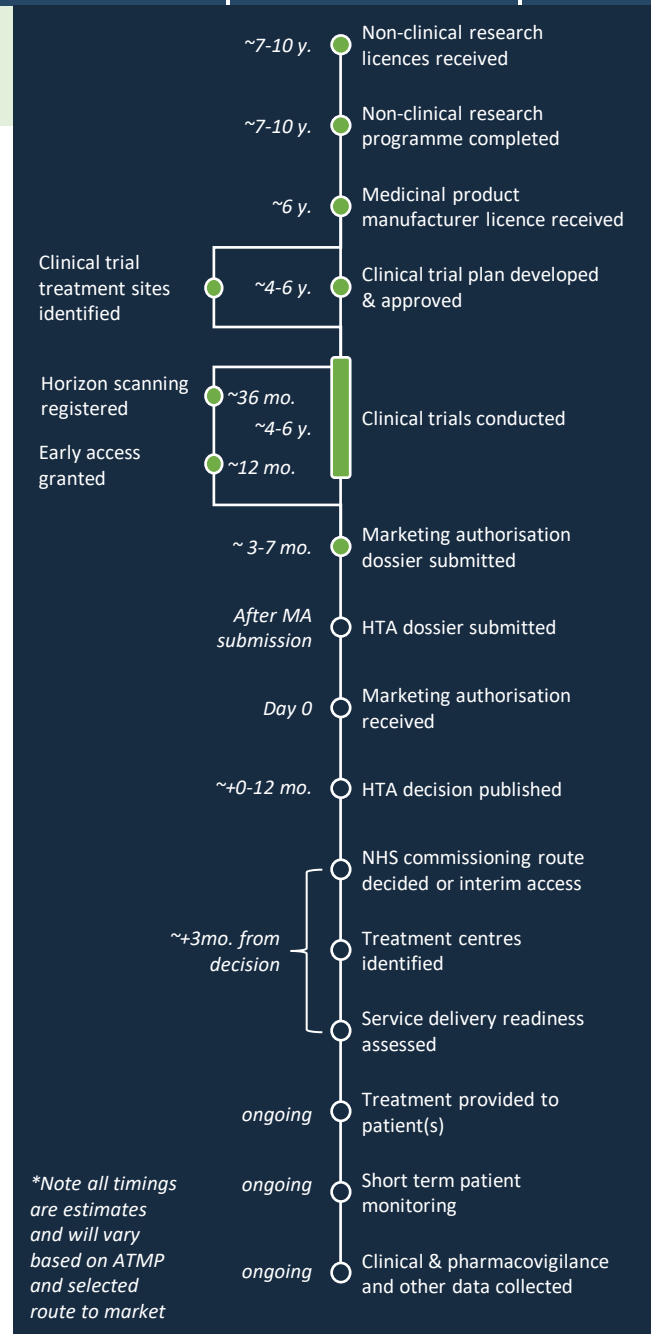
## To-do list

## Output

- ATMP developer
- NICE
- HSCB
- DHSC

Linked steps | Who is involved? | Best practices & tips

Back to England TA | Back to England HST



## KEY TOPICS

**Implementation of NICE guidance in Northern Ireland**

Overview | To-do list | Output

Linked steps | Who is involved? | Best practices & tips | Back to England TA | Back to England HST

## KEY TOPICS

- **Patient Access Scheme [optional]**
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]

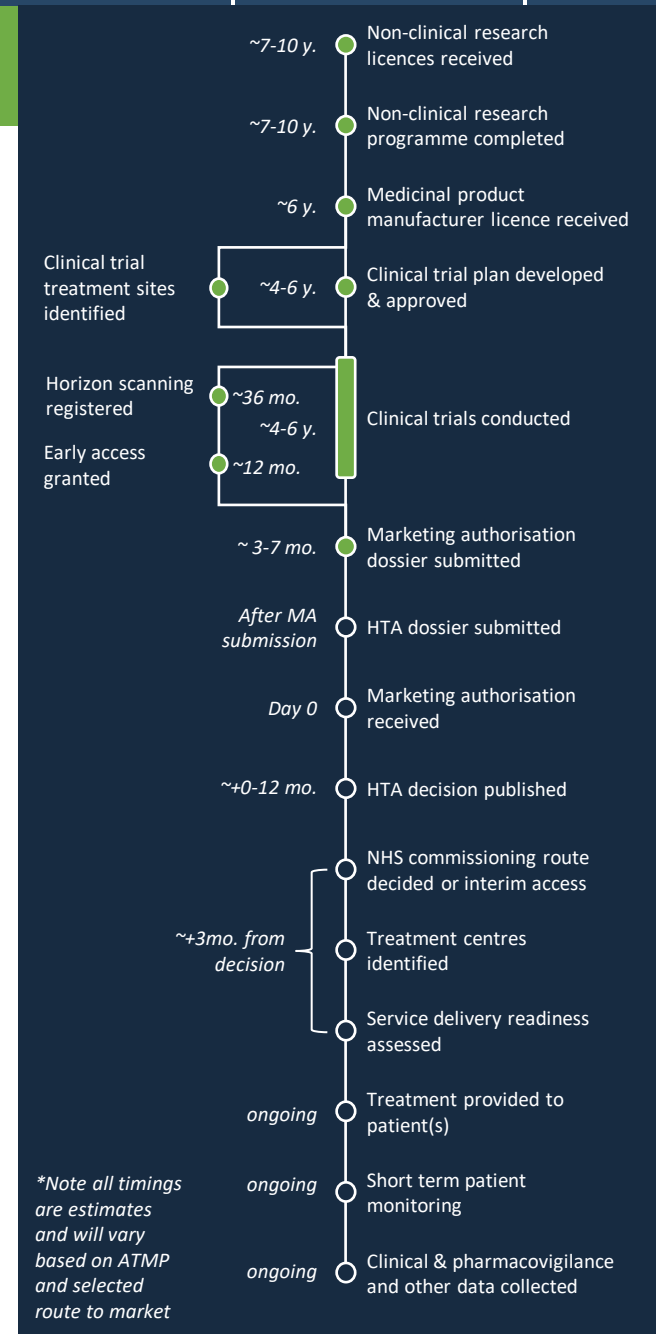
**Overview** | To-do list | Output

Patient access schemes are pricing agreements proposed by pharmaceutical companies. They aim to improve cost-effectiveness and enable patients to gain access to high cost drugs and treatments.

As a first step, developers should review the NHS commercial framework for new medicines to assess commercial options available and guiding principles. ATMP developers can propose either a simple or complex scheme to NHSE through the Patient Access Schemes Liaison Unit (PASLU – part of the NICE Commercial Liaison Team).

Developers can also request a commercial or clinical surgery with NHS England to facilitate further targeted discussions. Commercial surgeries are often used to discuss a complex PAS or commercial agreement, whereas clinical surgeries allow for interfacing with the specialised commissioning team. During the PAS discussions, the need for a Commercial Access Arrangement (CAA) may become apparent.





## KEY TOPICS

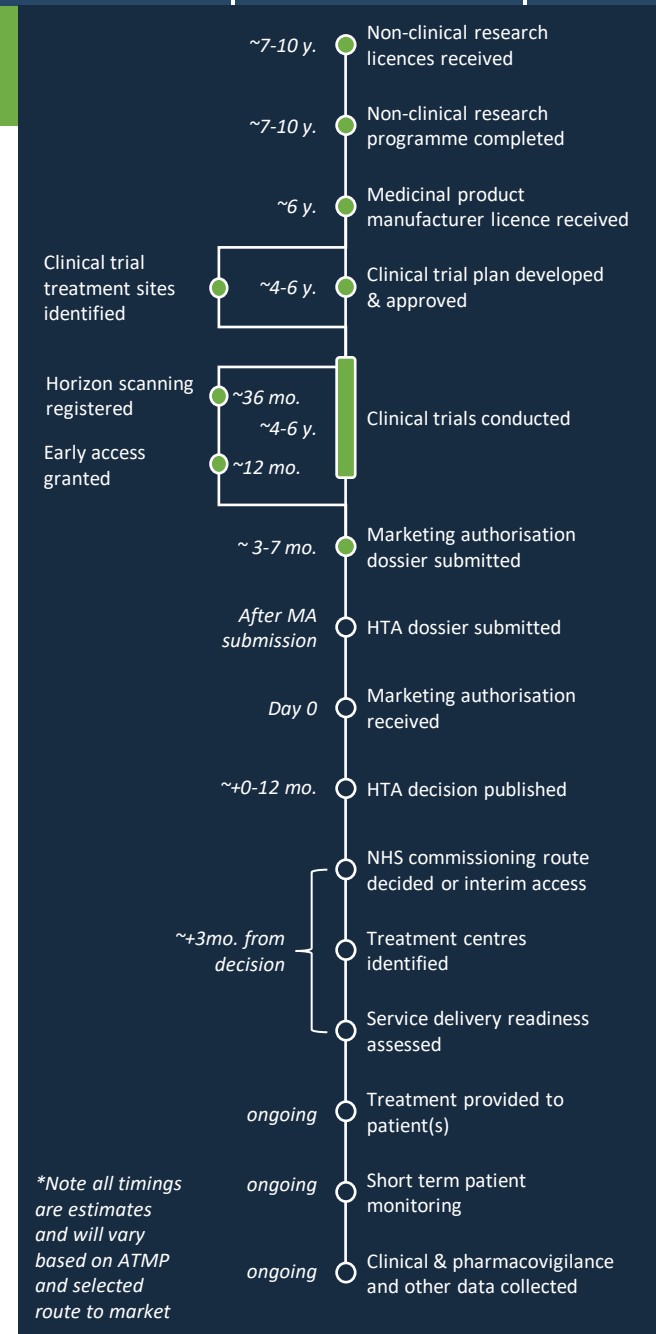
- **Patient Access Scheme [optional]**
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]

Overview | **To-do list** | Output

- Review NHS commercial framework for new medicines here
- Identify if scheme is simple or complex (see criteria here)
- Review PASLU procedure guide here
- Developer reaches out to NHSE about their proposed PAS scheme
- Contact PASLU at PASLUMail@nice.org.uk for an initial discussion about intention to submit a scheme
- Complete the proposal template, either for a complex scheme here or simple discount scheme here
  - Proposal template for complex scheme can be found here
  - Proposal template for simple scheme can be found here
- Submit the completed proposal template and any supporting documents to NHSE&I
- Attend expert panel meeting (complex PAS only)
- To propose a Wales Patient Access Scheme when going through the AWMSG appraisal process, review guidance from AWMSG here

**When**
Approval for PAS must be received prior to HTA evidence submission (however simple PAS may be proposed later in the process under exceptional circumstances)

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



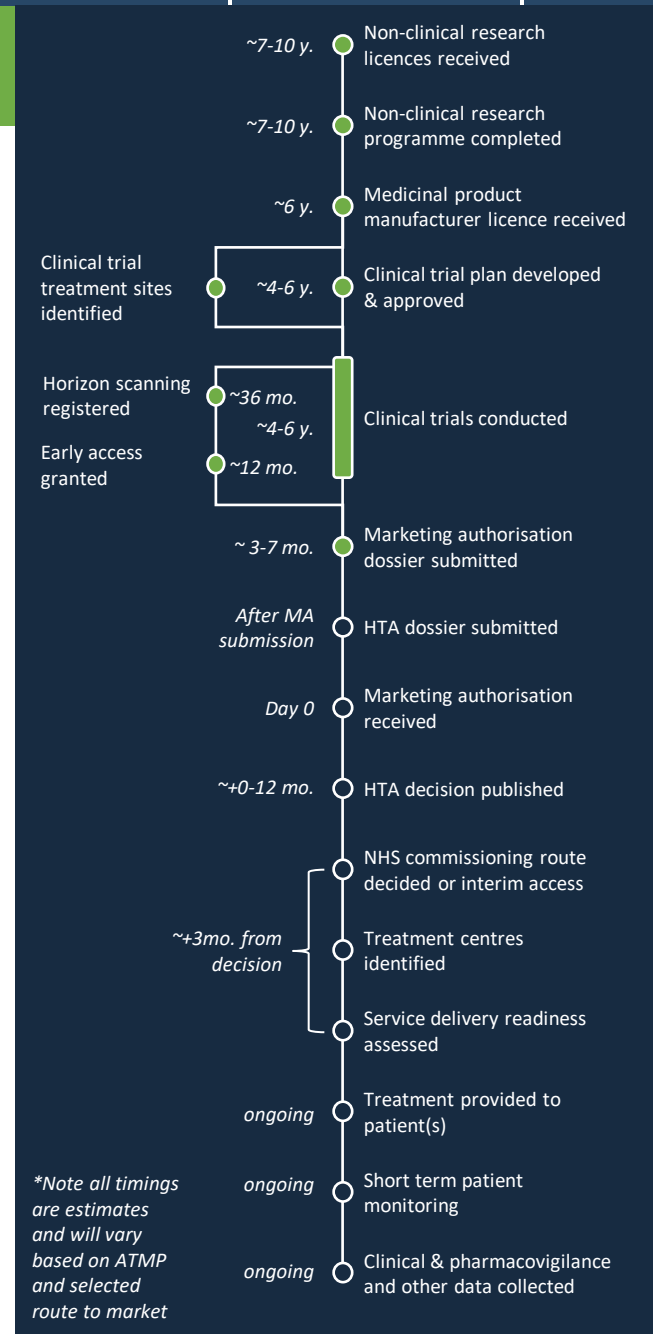
## KEY TOPICS

- **Patient Access Scheme [optional]**
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]

Overview | To-do list | **Output**

- NHS England final decision on inclusion of simple or complex PAS in TA or HST programme

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



1 What programmes are available to accelerate time to market?

2 How can an ATMP obtain early access through EAMS?

3 What are the routes for ATMP reimbursement assessment?

4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

- **Patient Access Scheme [optional]**
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]

## Overview

Health Technology Assessment Technology Appraisal

Health Technology Assessment Highly Specialised Technologies evaluation

Commercial Access Agreement [optional]

Managed Access Agreement [optional]

Service delivery readiness

## To-do list

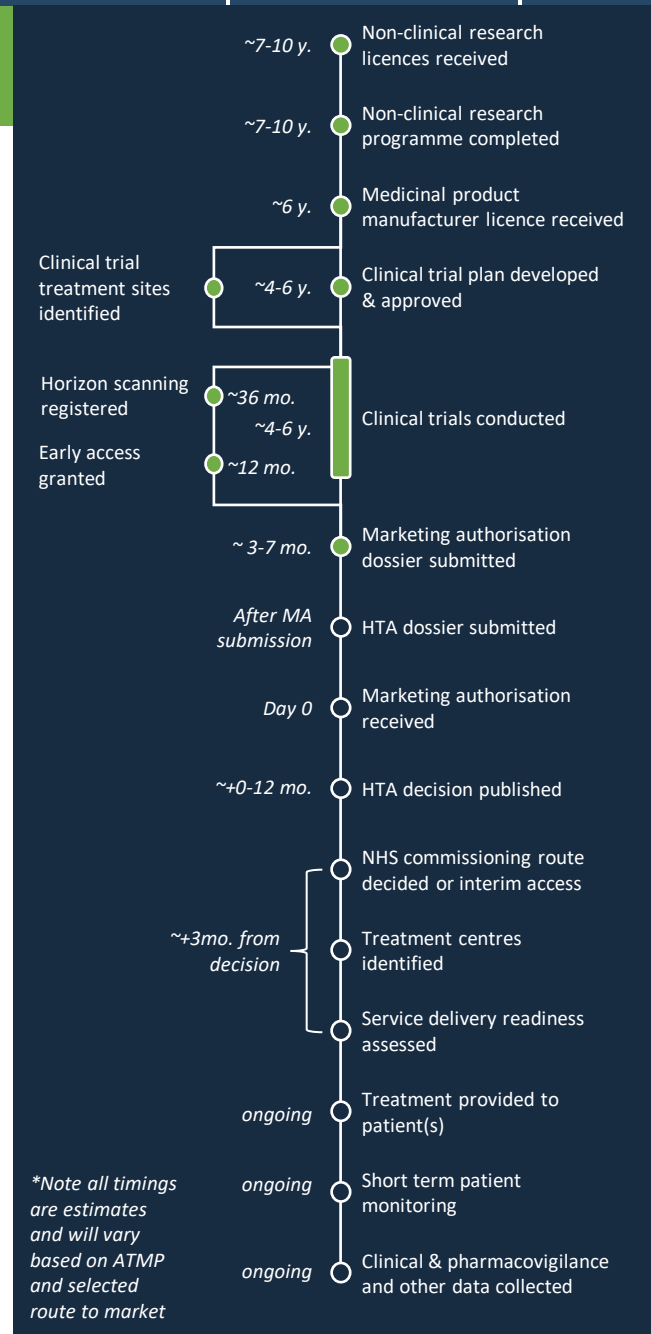
## Output

**Linked steps**

**Who is involved?**

**Best practices & tips**

**Variation by devolved nation**



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4 What reimbursement commercial arrangement options are available?

## KEY TOPICS

- **Patient Access Scheme [optional]**
- Commercial Access Agreement [optional]
- Managed Access Agreement [optional]

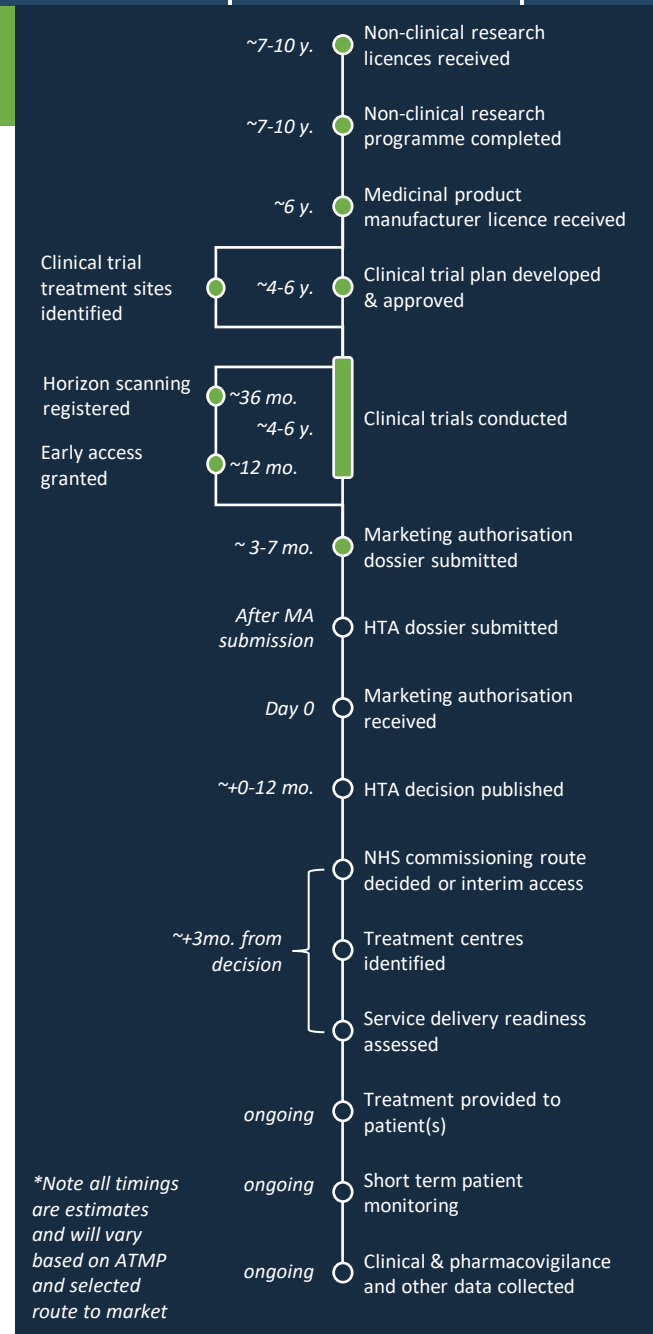
## Overview

## To-do list

## Output

- ATMP developer
- PASLU (NICE)
- NHSE

**Linked steps** | **Who is involved?** | **Best practices & tips** | **Variation by devolved nation**



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## KEY TOPICS

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- Managed Access Agreement [optional]

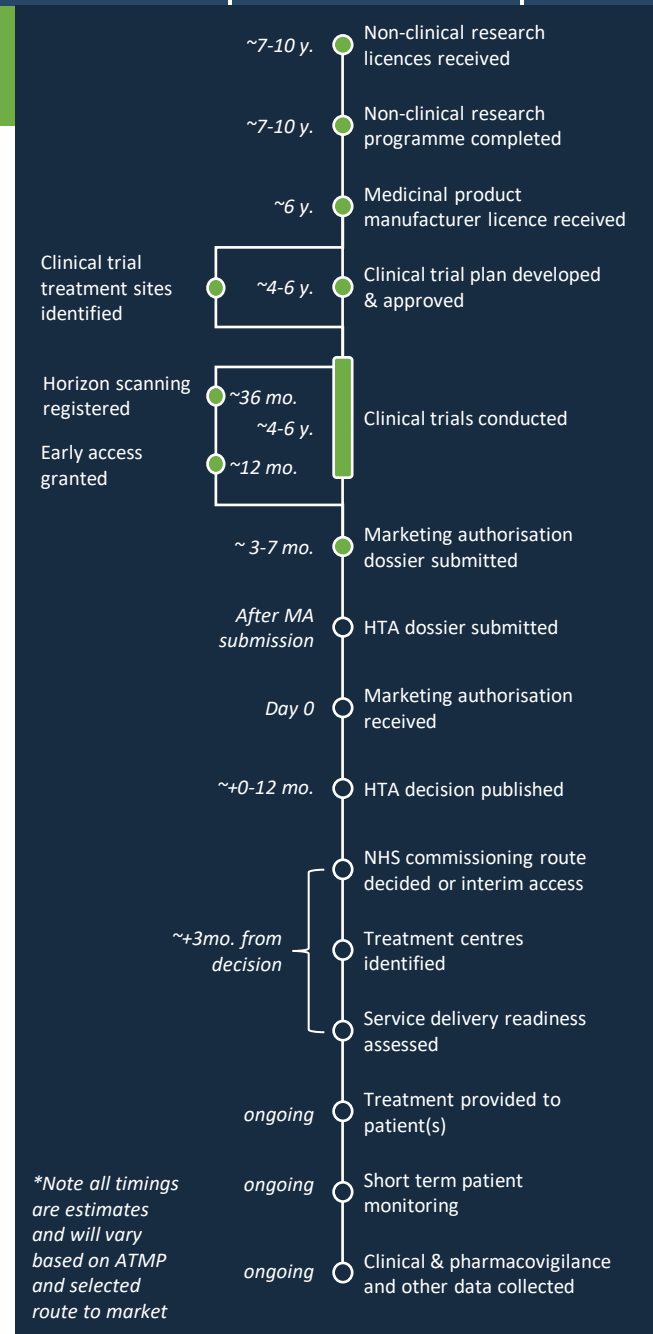
## Overview

## To-do list

## Output

- Simple PAS schemes are typically faster to implement, however if pursuing a complex PAS, developers should be mindful of the data capabilities and infrastructure of the NHS to avoid additional burden of further data collection

Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation



## KEY TOPICS



**Overview** | To-do list | Output

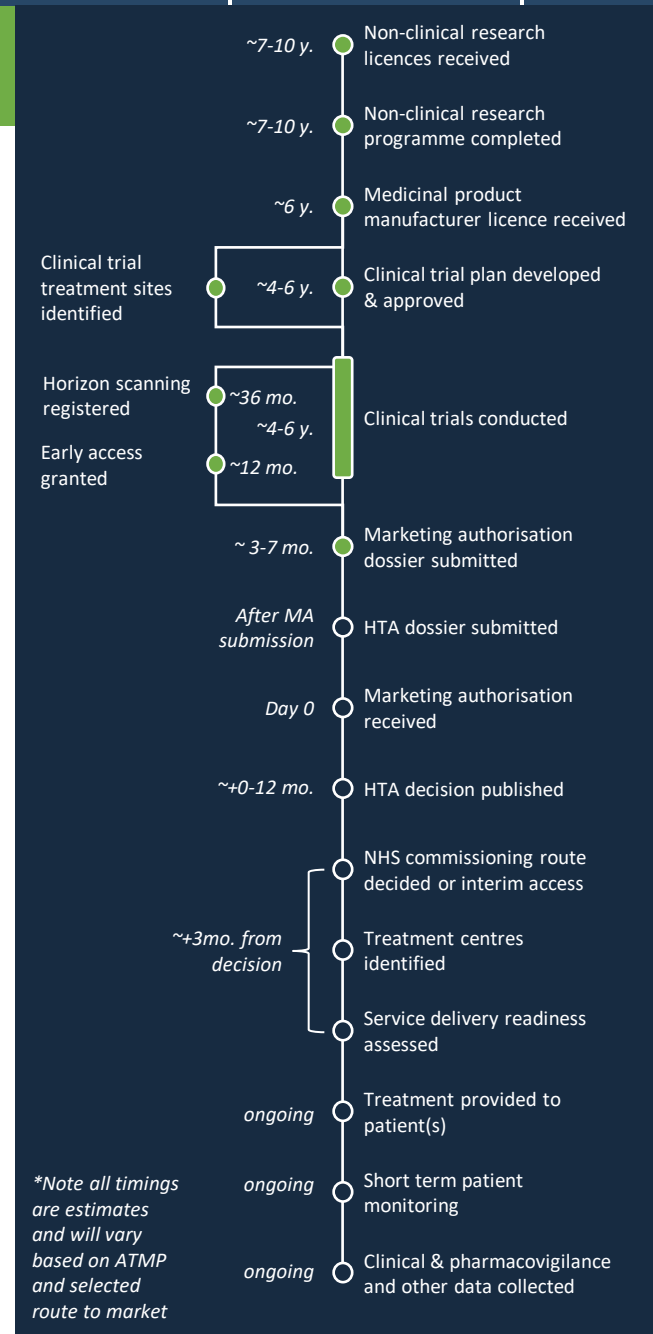
Developers should review the NHS commercial framework for new medicines to assess commercial options available and guiding principles.

Unlike patient access scheme arrangements, Commercial Access Agreements (CAA) are only expected to be used in specific circumstances, and can provide companies with an additional confidential commercial mechanism to improve the likely cost effectiveness of a medicine. They can be used alone or in combination with a patient access scheme (PAS).

If interested in submitting a CAA (which can be done at various checkpoints listed here), developers must liaise with NICE's Commercial Liaison Team and the Commercial Medicines Directorate at NHSE to assess the potential for such a request. Note that a request can only be submitted if a PAS proposal has been fully explored.

NICE will review and filter requests and develop a commercial briefing for joint discussion with NHSE. Accepted CAA requests will be considered by NICE committee in the HTA appraisal process.

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

- Patient Access Scheme [optional]
- **Commercial Access Agreement [optional]**
- Managed Access Agreement [optional]

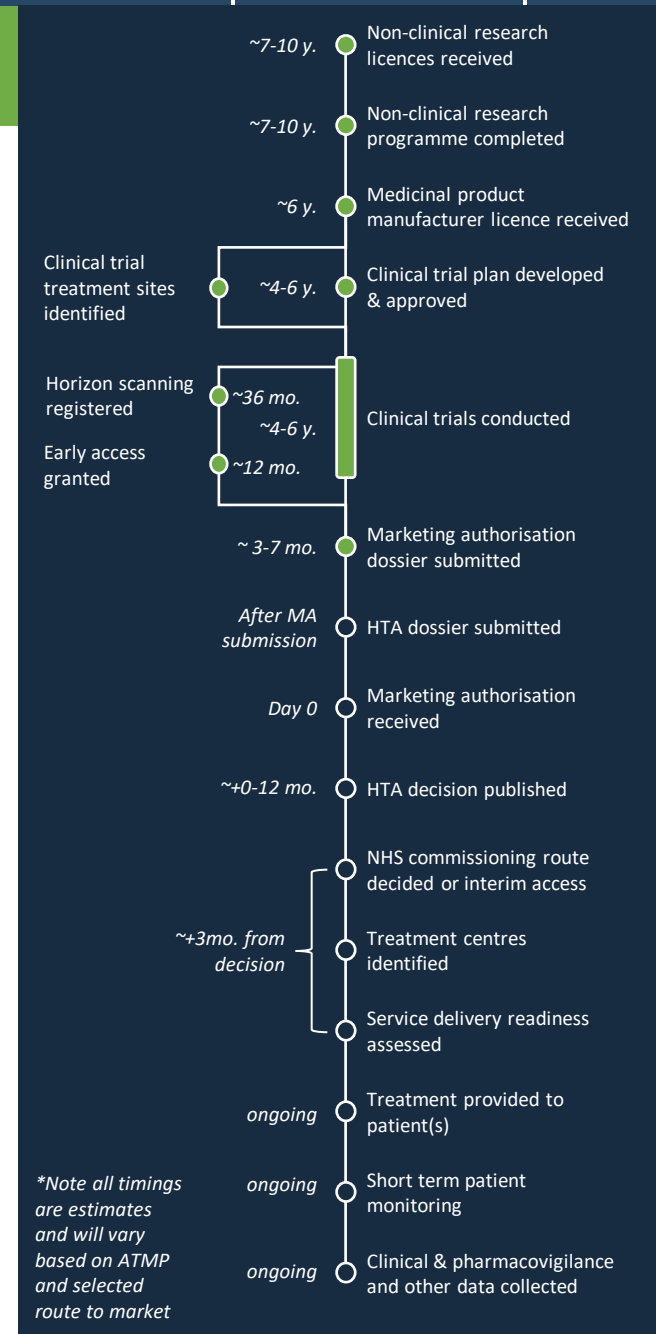
Overview | **To-do list** | Output

- Review NHS commercial framework for new medicines here
- Review NICE process guide on requesting a CAA here
- Review guidance from ATTC on commercial arrangements here
- Discuss feasibility of CAA request with the commercial liaison team at NICE (CLPT@nice.nhs.uk) and consult the Commercial Medicines Directorate at NHSE (england.commercialmedicines@nhs.net)
- Submit CAA request
- Develop CAA proposal for consideration in the HTA appraisal process

**When**

Prior to or during HTA appraisal/evaluation process

Linked steps | Who is involved? | Best practices & tips



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4 What reimbursement commercial arrangement options are available?

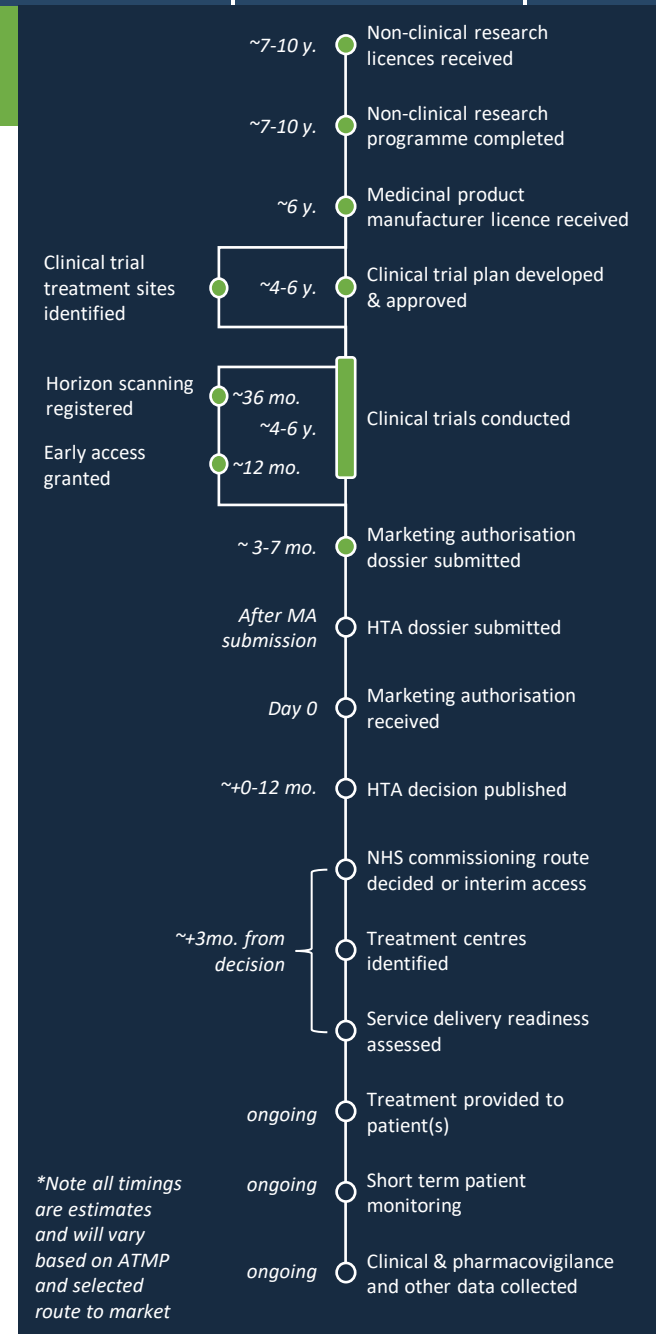
## KEY TOPICS

- Patient Access Scheme [optional]
- **Commercial Access Agreement [optional]**
- Managed Access Agreement [optional]

Overview | To-do list | **Output**

- Submission of confidential CAA to NHSE
- Confidential Commercial Access Agreement included in evidence submission

Linked steps | Who is involved? | Best practices & tips



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## KEY TOPICS

- Patient Access Scheme [optional]
- **Commercial Access Agreement [optional]**
- Managed Access Agreement [optional]

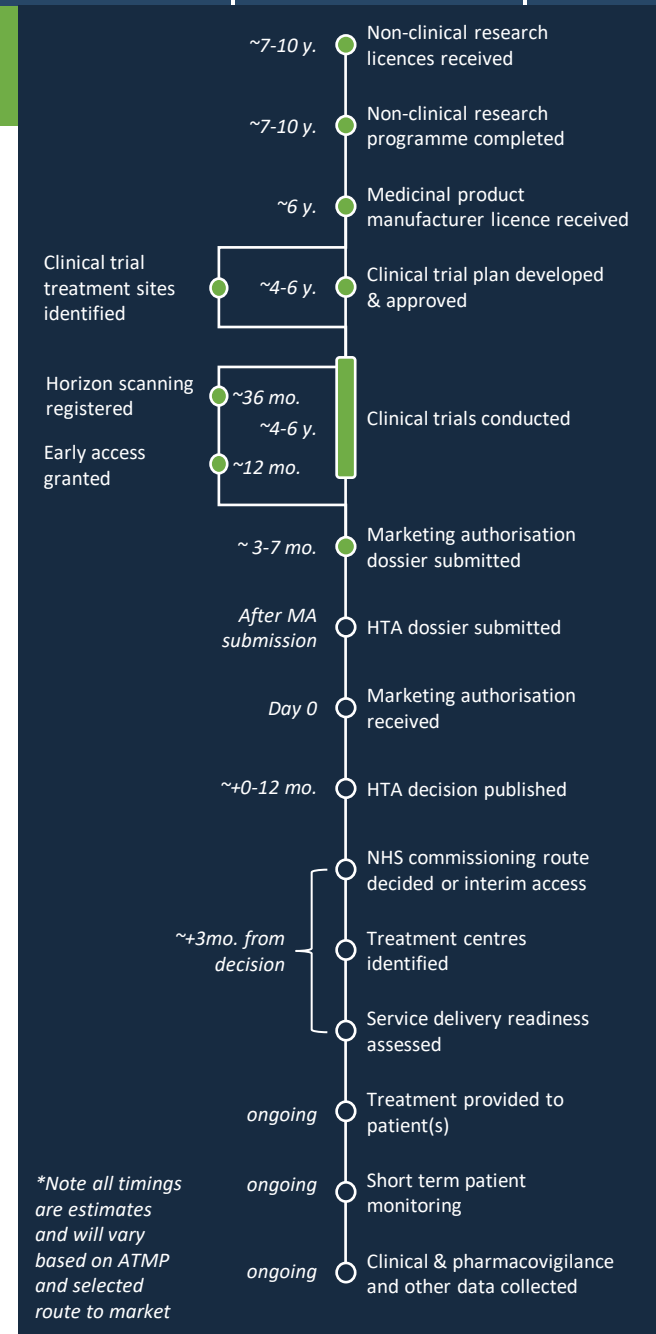
## Overview

## To-do list

## Output

- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation
- Patient Access Scheme [optional]
- Managed Access Agreement [optional]
- Service delivery readiness

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Patient Access Scheme [optional]
- **Commercial Access Agreement [optional]**
- Managed Access Agreement [optional]

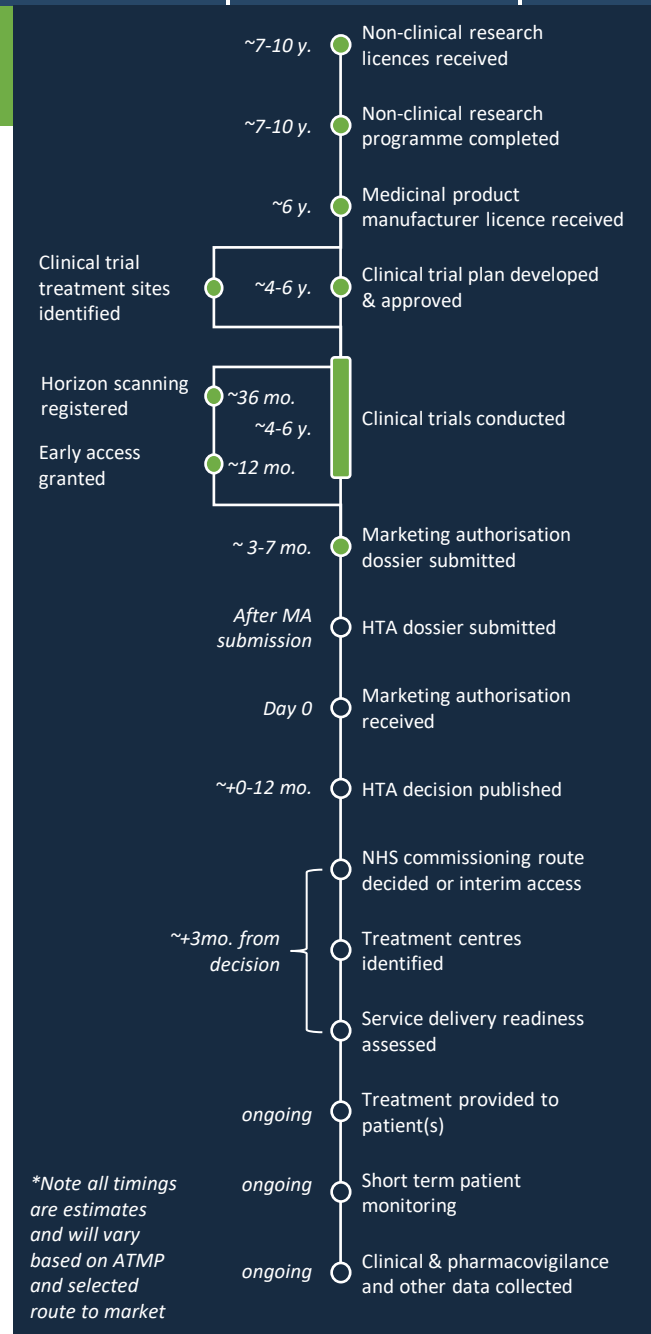
## Overview

## To-do list

## Output

- ATMP developer
- NICE
- NHSE

**Linked steps** **Who is involved?** **Best practices & tips**



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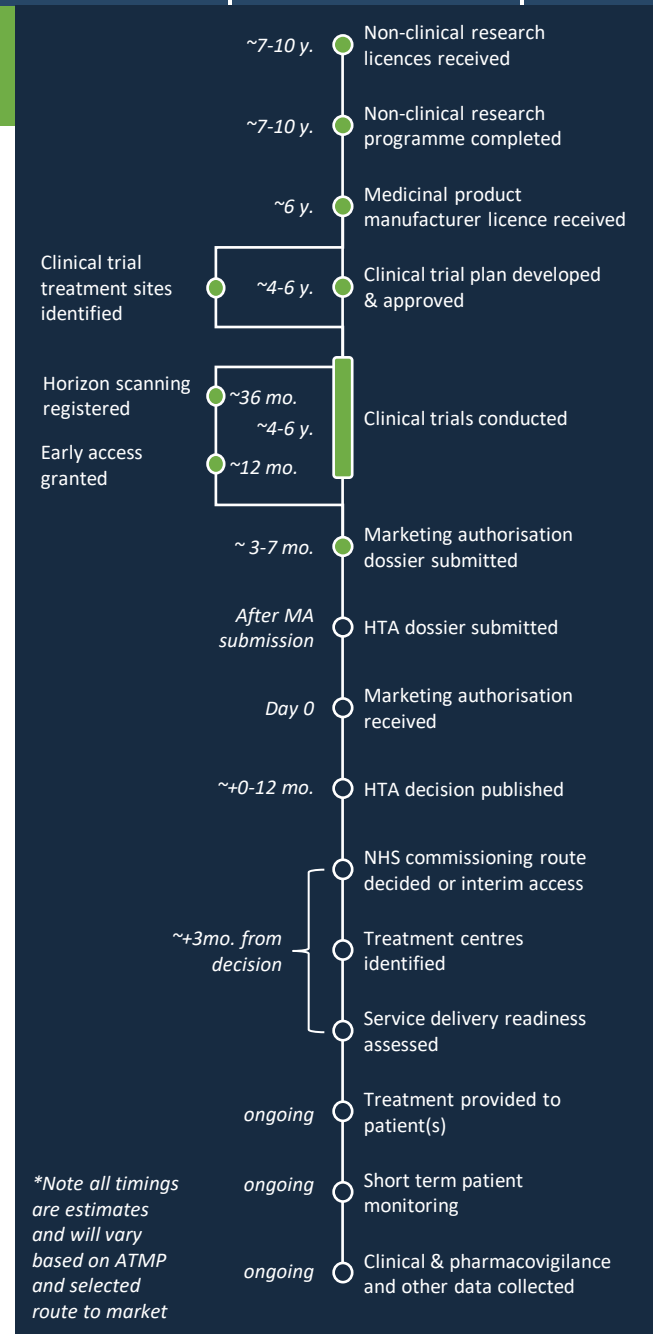
Overview | To-do list | Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



## KEY TOPICS



**Overview** | To-do list | Output

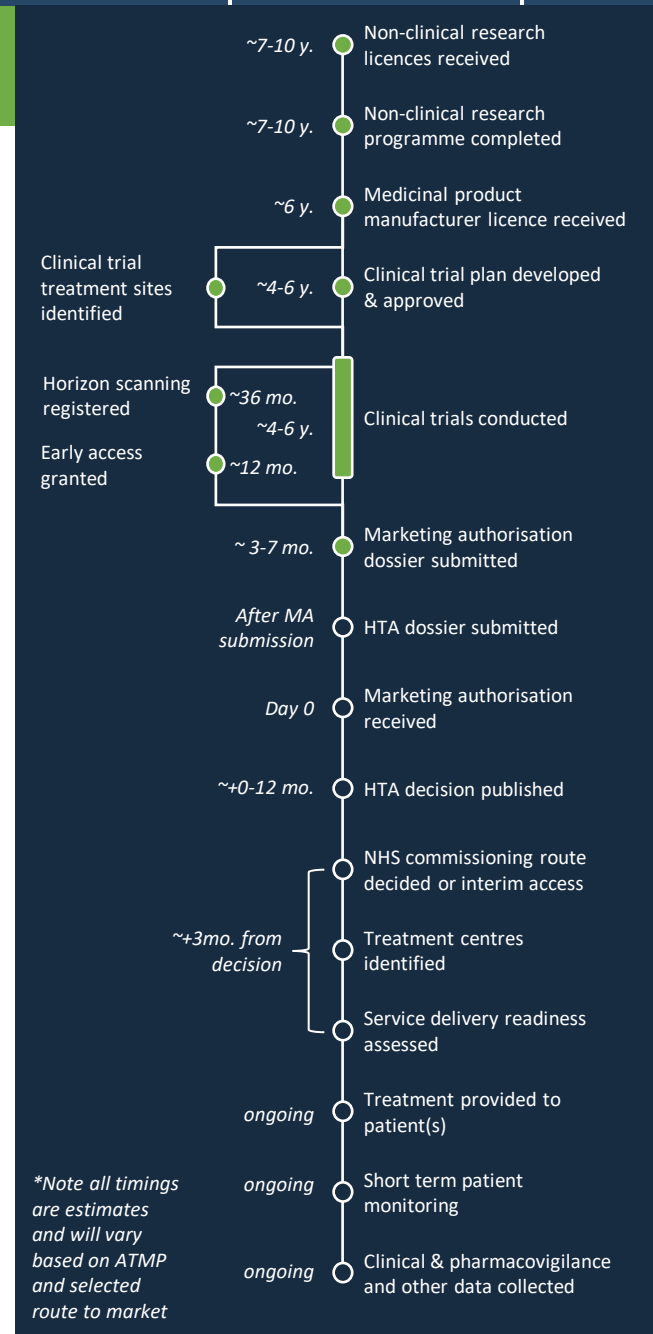
Developers should review the NHS commercial framework for new medicines to assess commercial options available and guiding principles. Unlike patient access scheme arrangements, MAA are only expected to be used in specific circumstances. Following a Managed Access recommendation by NICE, a Managed Access Agreement enables further exploration between NHSE & the developer of the clinical and financial uncertainty remaining for a medicine.

MAAs consist of two key components: a data collection agreement to mitigate clinical uncertainty (as defined by the NICE Committee), and either a PAS or a PAS + CAA. MAAs require the developer's agreement to offer the treatment at a cost-effective price for the duration of the MAA. There are exit clauses in place as part of each MAA, including the obligation to maintain funding and existing patient access should any reassessment result in a negative decision.

If interested in submitting a request for a MAA (which can be done at various checkpoints listed here), developers must liaise with NICE's commercial liaison team and the Commercial Medicines Directorate at NHSE&I to assess the potential for such a request. Note that a request can only be submitted if a PAS proposal has been fully explored.

**Next >**

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS



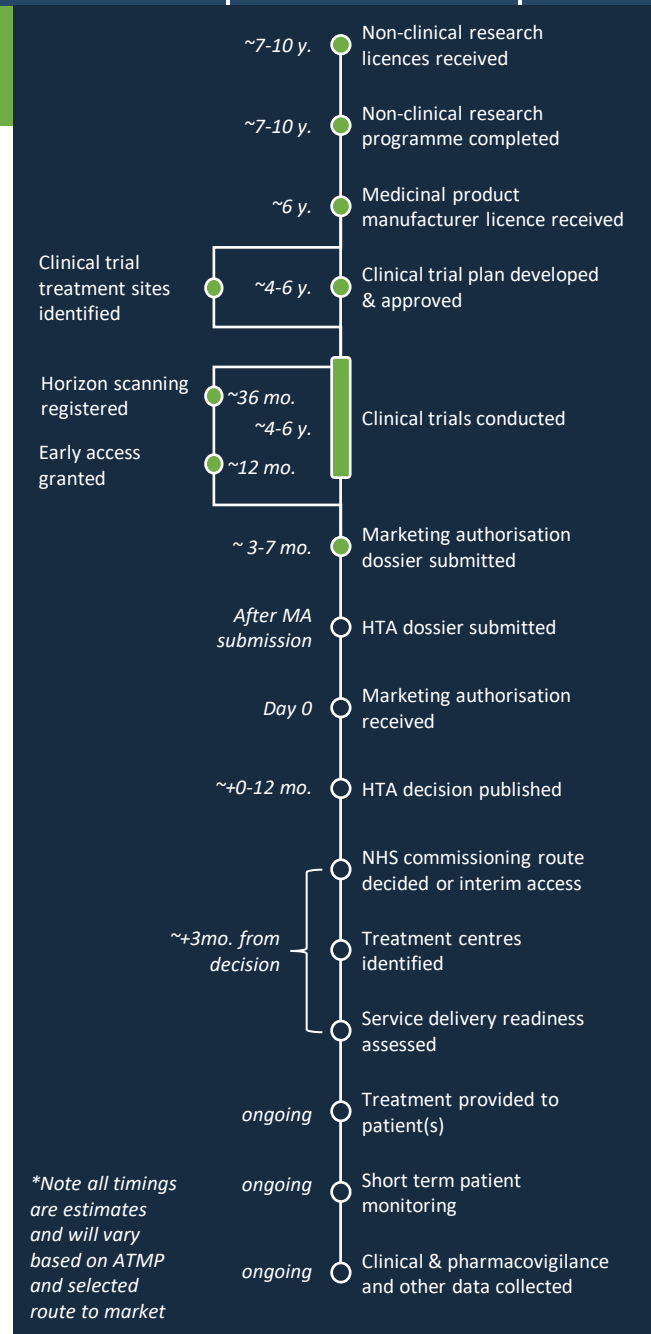
**Overview** | To-do list | Output

NICE will review and filter requests and develop a commercial briefing for joint discussion with NHSE&I. Accepted MAA requests will be considered by NICE committee in the HTA appraisal process.

At the end of a MAA, a NICE reappraisal will take place, taking into account additional data and (if applicable) the newly proposed price. MAA are most frequently used in the context of the CDF (and are expected to be used with the forthcoming Innovative Medicines Fund (IMF) however NICE is able to recommend Managed Access for any medicine.

**< Previous**

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

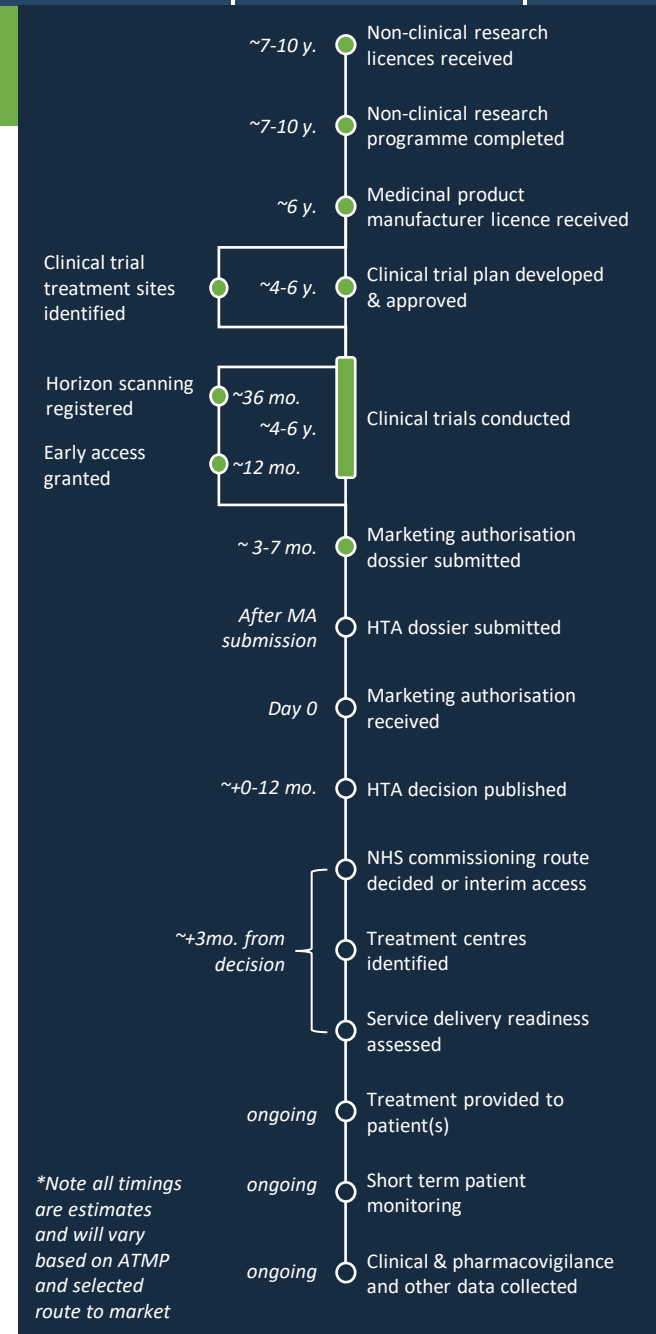
- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- **Managed Access Agreement [optional]**

Overview | **To-do list** | Output

- Review NHS commercial framework for new medicines here
- Review NICE process guide on MAA here
- Discuss proposed MAA with NHSE
- Submit proposal for Data Collection Arrangement
  - If doing MAA via the CDF, complete the CDF Commercial Agreement template
  - Review the CDF standard operating procedures here (if applicable – includes details on how the CDF operates)
- Submit proposed MAA as part of HST/TA evaluation and assessment

**When**
During HTA appraisal/evaluation process, if requested by NICE

Linked steps | Who is involved? | Best practices & tips



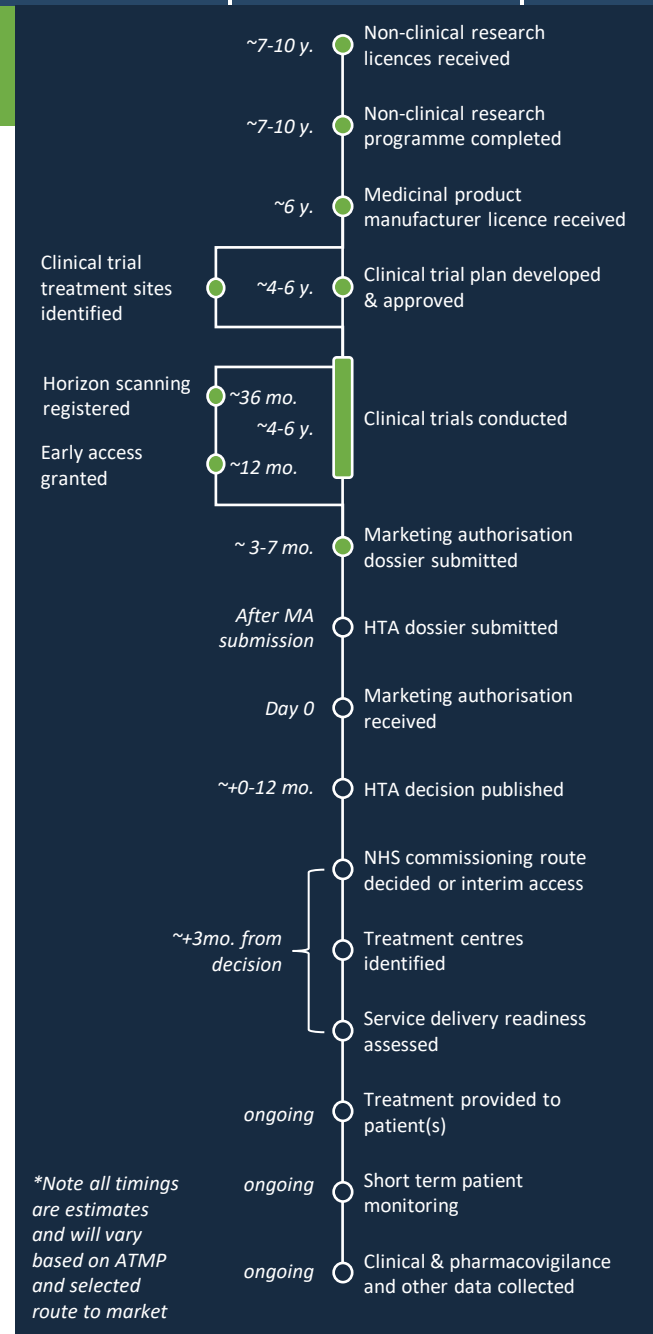
## KEY TOPICS



Overview | To-do list | **Output**

- Managed Access Agreement included in evidence submission

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- **Managed Access Agreement [optional]**

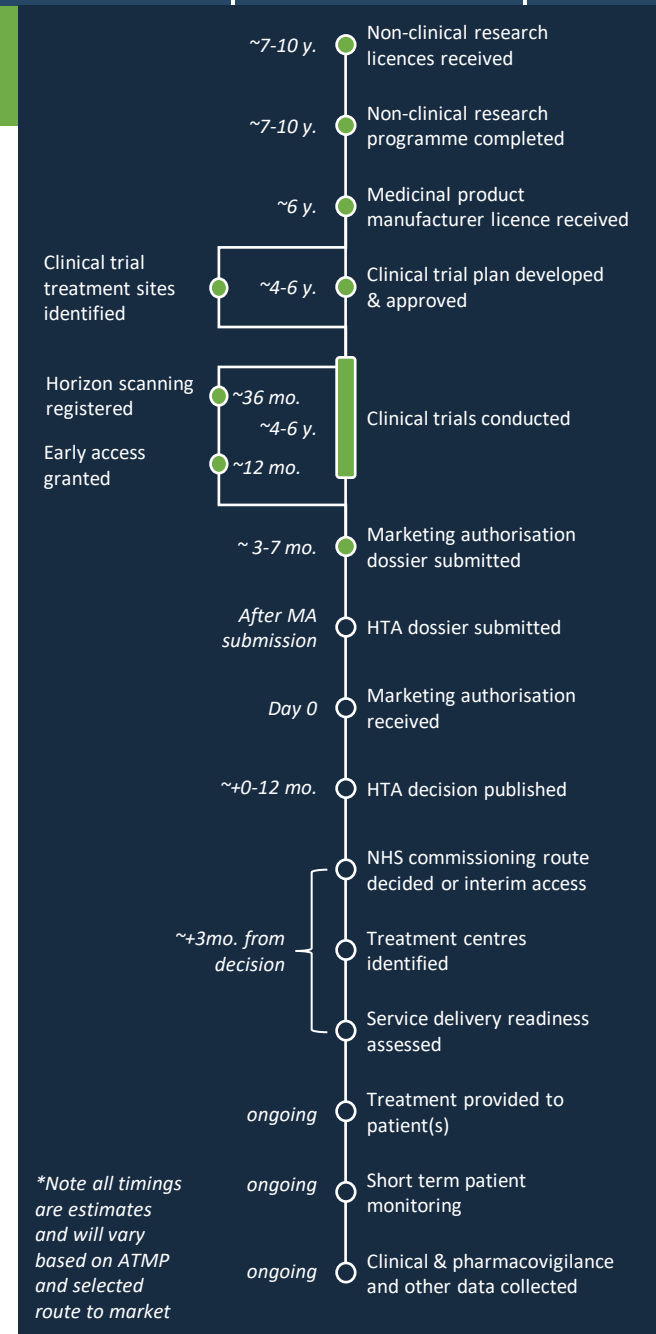
## Overview

## To-do list

## Output

- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation
- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- Service delivery readiness

**Linked steps** **Who is involved?** **Best practices & tips**



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## KEY TOPICS

- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- **Managed Access Agreement [optional]**

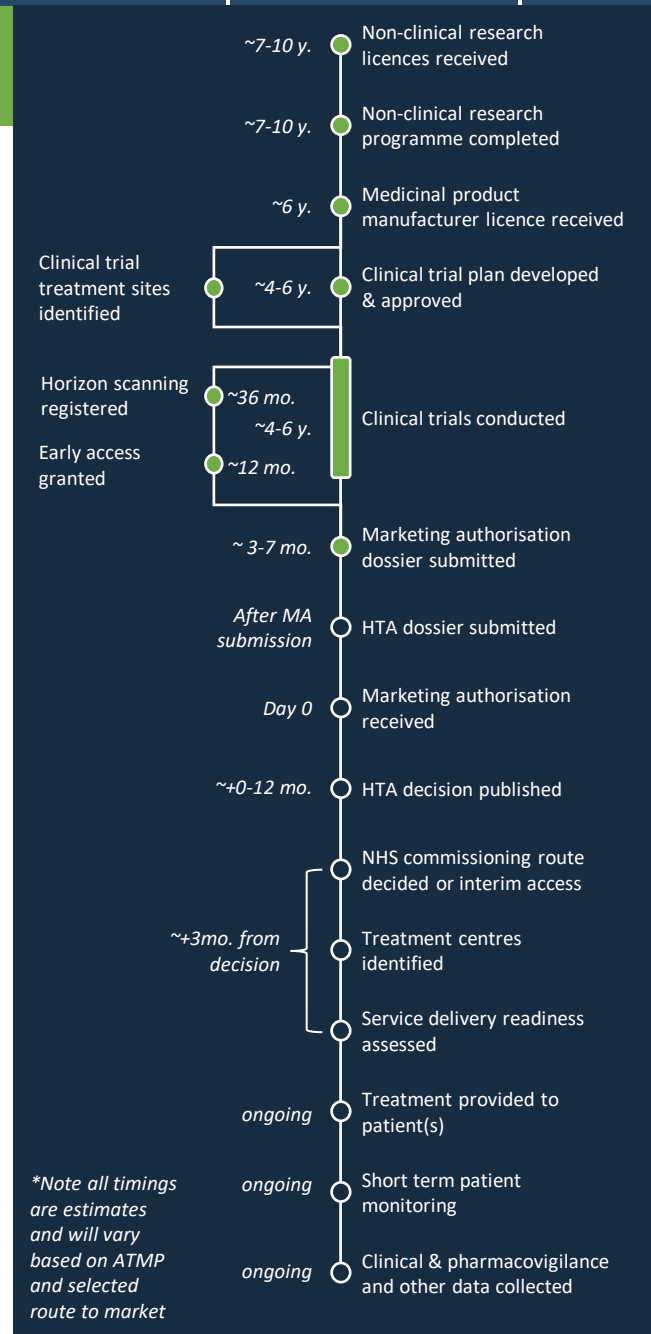
## Overview

## To-do list

## Output

- ATMP developer
- NICE
- NHSE&I
- Cancer Drugs Fund (and future IMF)

**Linked steps** **Who is involved?** **Best practices & tips**



## KEY TOPICS

- Patient Access Scheme [optional]
- Commercial Access Agreement [optional]
- **Managed Access Agreement [optional]**

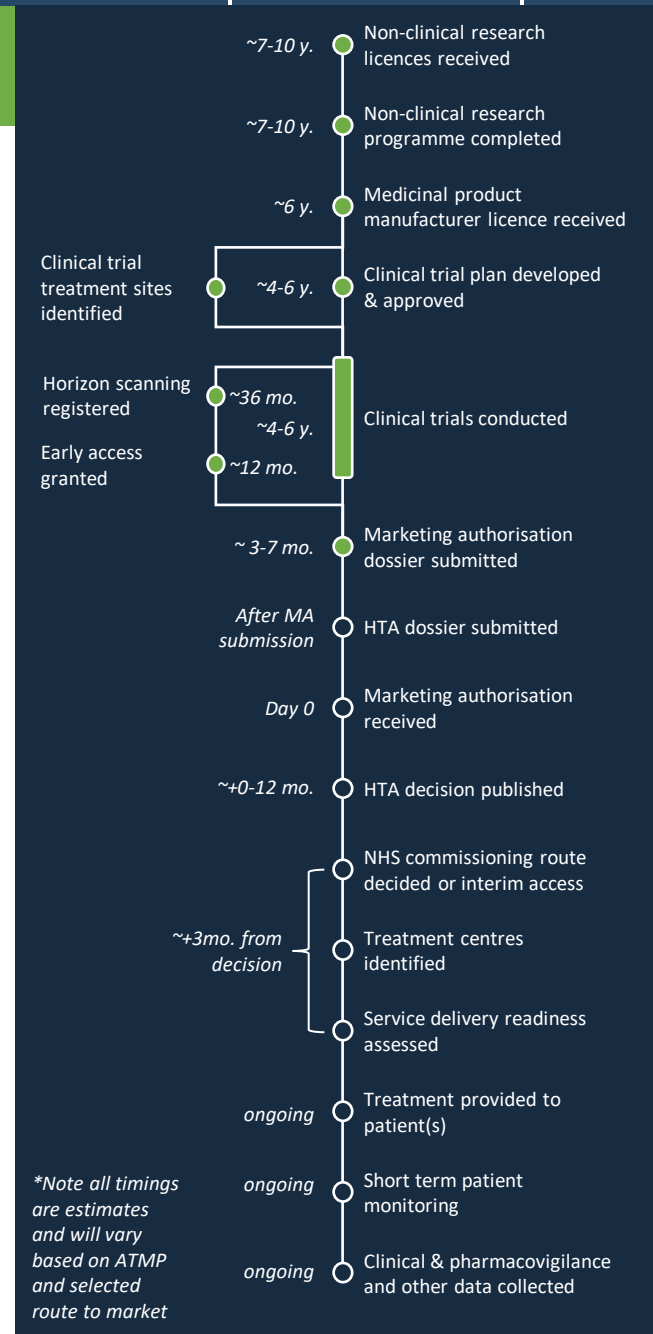
## Overview

## To-do list

## Output

- For the data collection agreement, ensure that any outcomes used are captured through NHS systems and that the NHS data infrastructure and data quality is sufficient for the management of the MAA
- Developers may also consider supporting the NHS with development of the required digital infrastructure
- If intending to pursue a MAA, Developers should signal this intent along with proposed format as early as possible

Linked steps | Who is involved? | Best practices & tips



## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

**Overview** | To-do list | Output

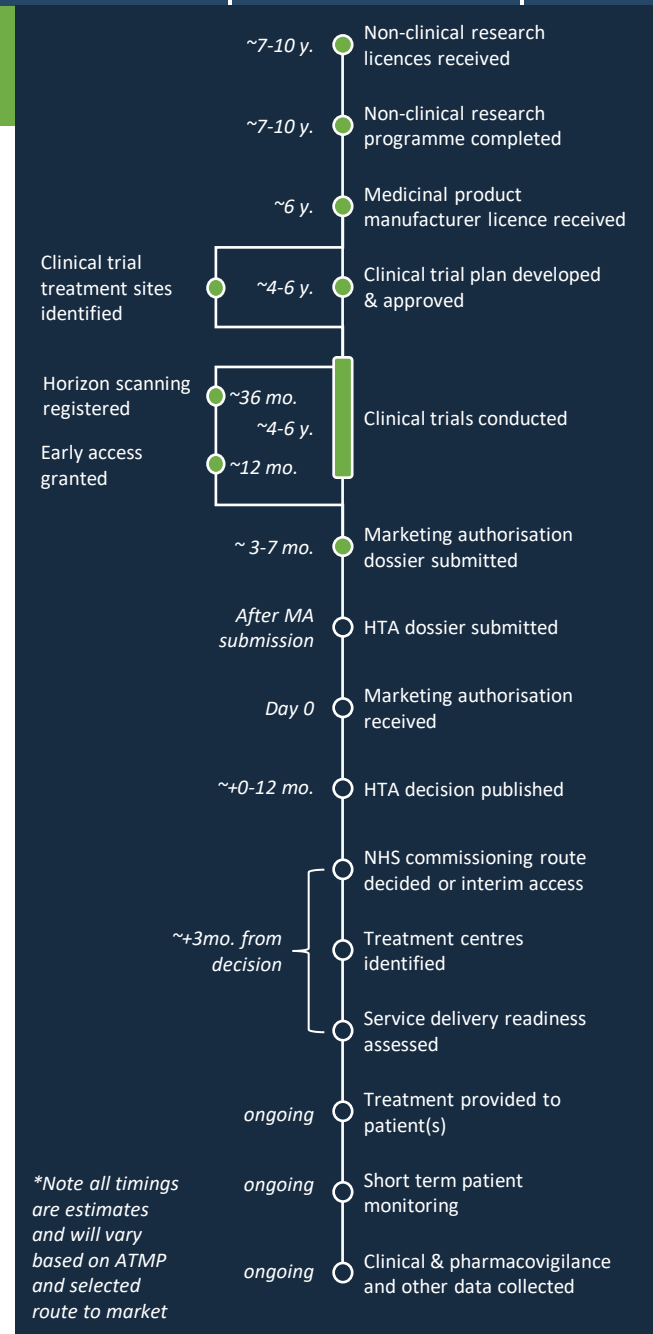
Developers should review the guidance from the Patient Access Scheme Assessment Group (PASAG) and identify if they intend to submit a concise (simple) or full (complex) PAS application.

The PAS application will be sent to the SMC Secretariat as part of the developers HTA submission documentation (or updated PAS may be sent following an SMC New Drugs Committee meeting). The SMC Secretariat forward relevant documentation to the PASAG Secretariat.

The Scheme will be assessed using PAS principles, feedback from NHS Health Boards on operational feasibility of the scheme (as appropriate) and clarification questions may be sent to the developer.

If the PAS scheme is approved it will be included in the HTA submission, or if the PAS scheme is not recommended the list price will be used in the HTA.

Linked steps | Who is involved? | Best practices & tips | Back to England



## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

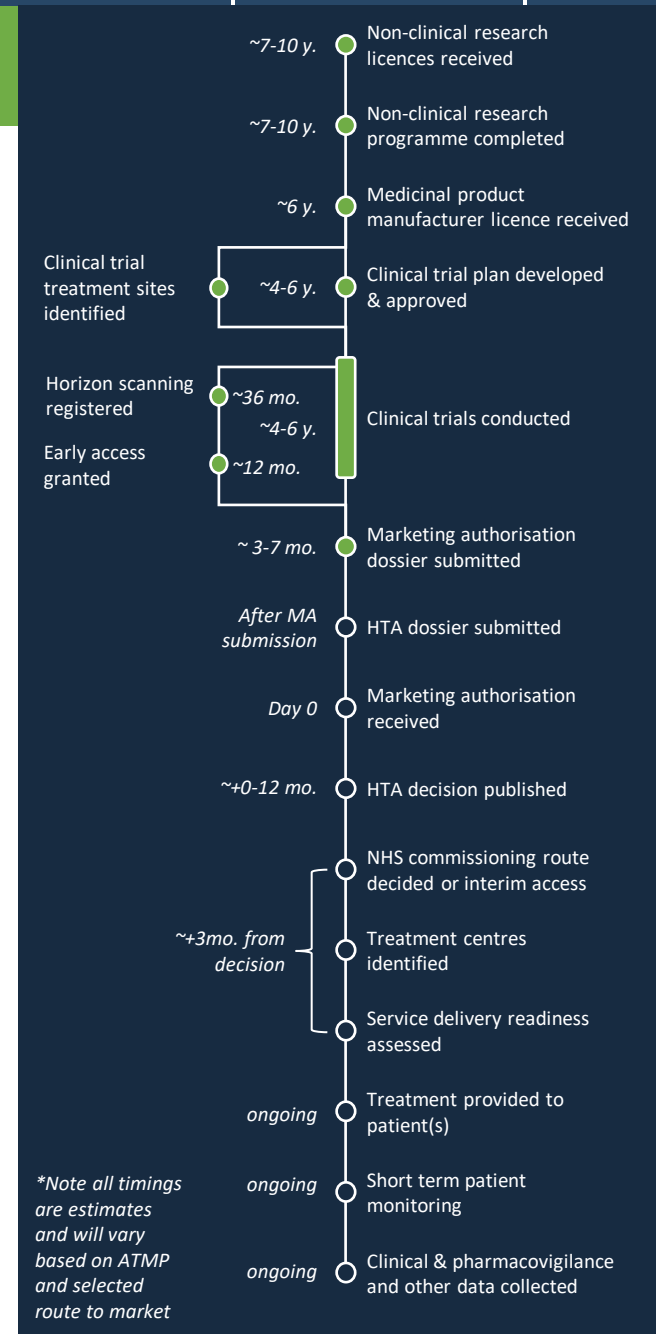
Overview | **To-do list** | Output

- Introduction to PAS from the SMC can be found here
- Identify if scheme is simple or complex by reviewing NHS Scotland PAS guidance here
  - Concise (simple) PAS application form here
  - Full (complex) PAS application form here

**When**

- PAS submission will form part of HTA evidence submission
- The concise (simple) scheme assessment takes approximately 4 weeks
- The full (complex) scheme assessment takes approximately 8 weeks





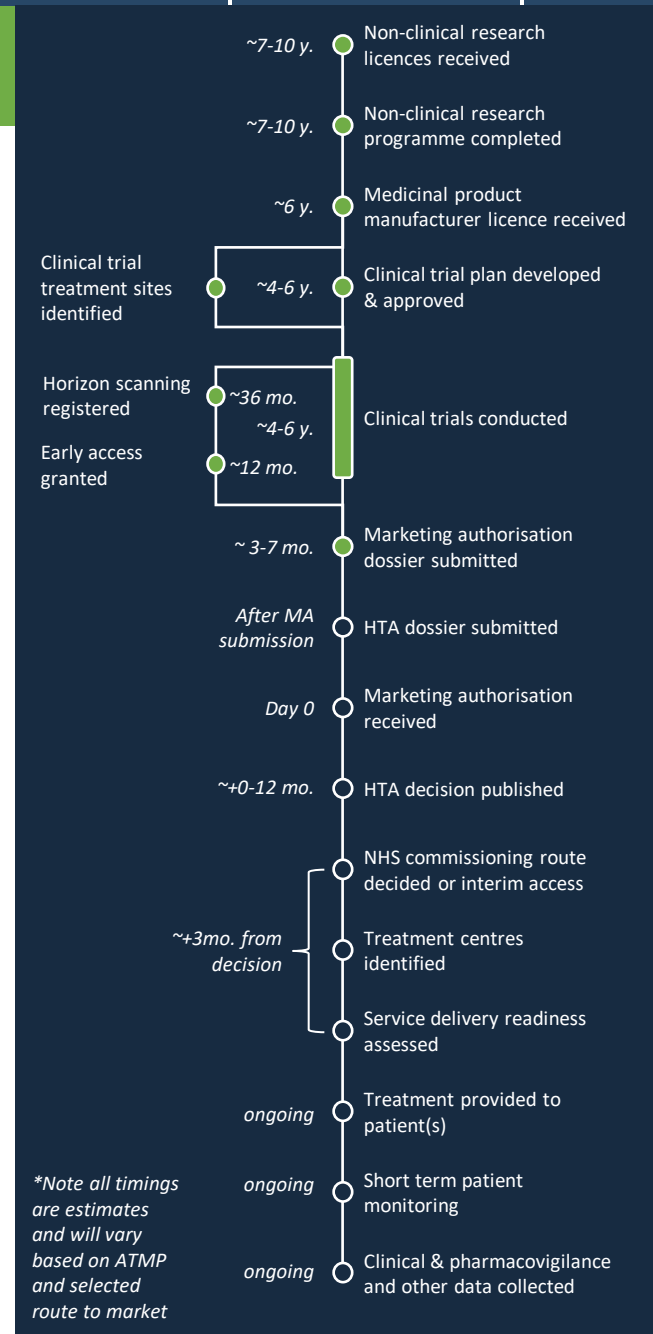
## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

Overview | To-do list | **Output**

- For both concise (simple) & full (complex) PAS, approval decisions are communicated separately to the HTA decision





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## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

Overview

To-do list

Output

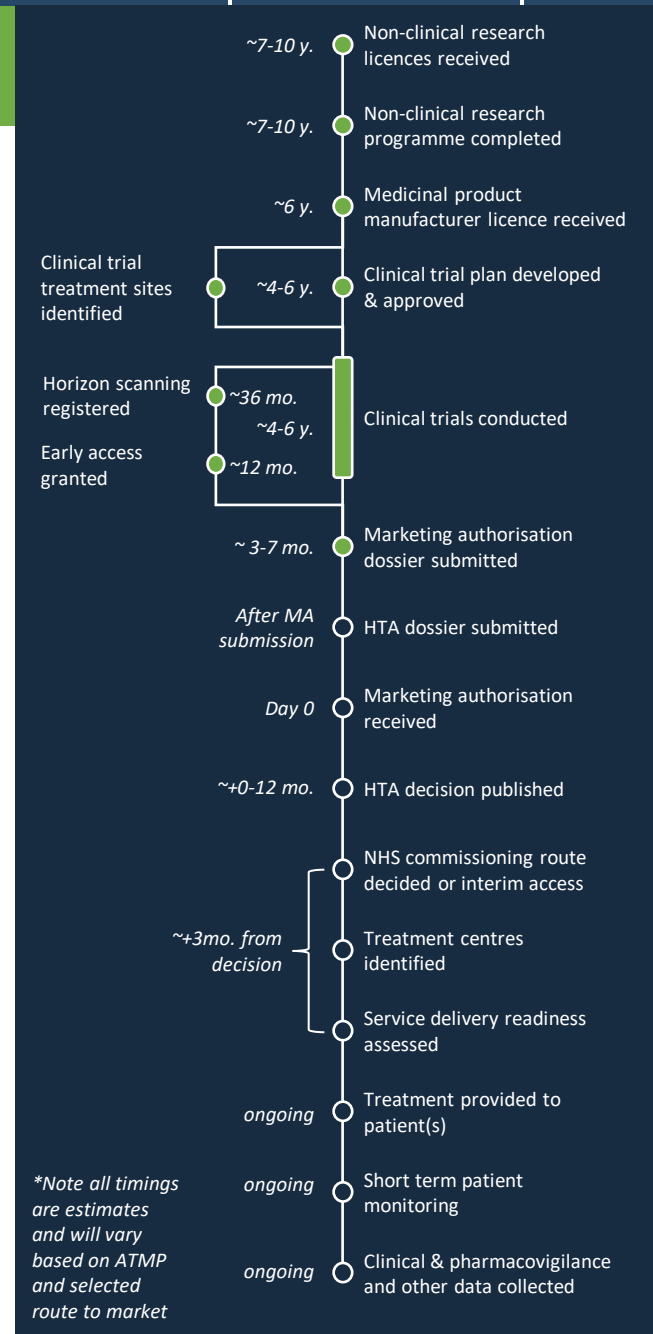
Service delivery readiness

Linked steps

Who is involved?

Best practices & tips

Back to England



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## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

## Overview

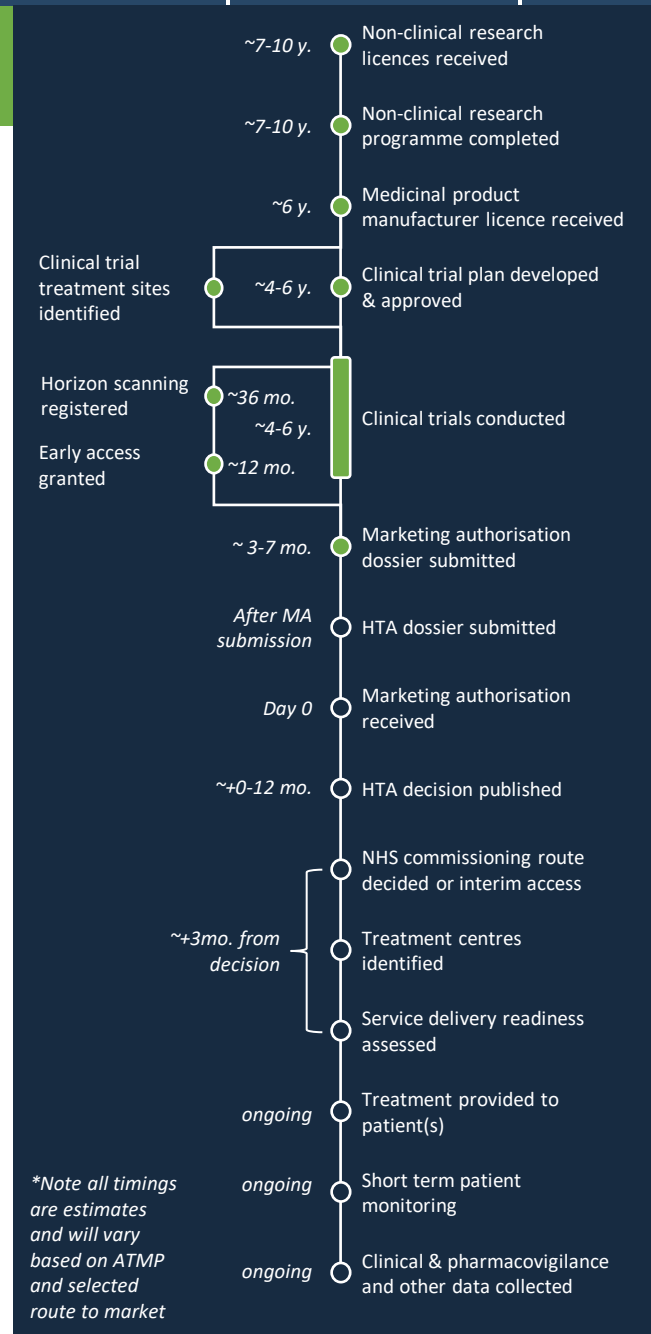
- ATMP developer
- PASAG

## To-do list

## Output

Linked steps | Who is involved? | Best practices & tips

**Back to England**



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## KEY TOPICS

**Patient Access Scheme [optional] – Scotland**

Overview | To-do list | Output


Linked steps | Who is involved? | Best practices & tips | Back to England

# 1 How are ATMPs commissioned?

## KEY TOPICS

- **Routine commissioning**
- Commissioning via Managed Access

**Overview** | To-do list | Output

Once a product has been assessed by NICE (through TA or HST) and receives a positive recommendation for routine commissioning, ATMPs are typically commissioned nationally through the NHS specialised or highly specialised commissioning service.

For non-oncology products, funding will become available within 90 days of NICE issuing the TA or HST Guidance.

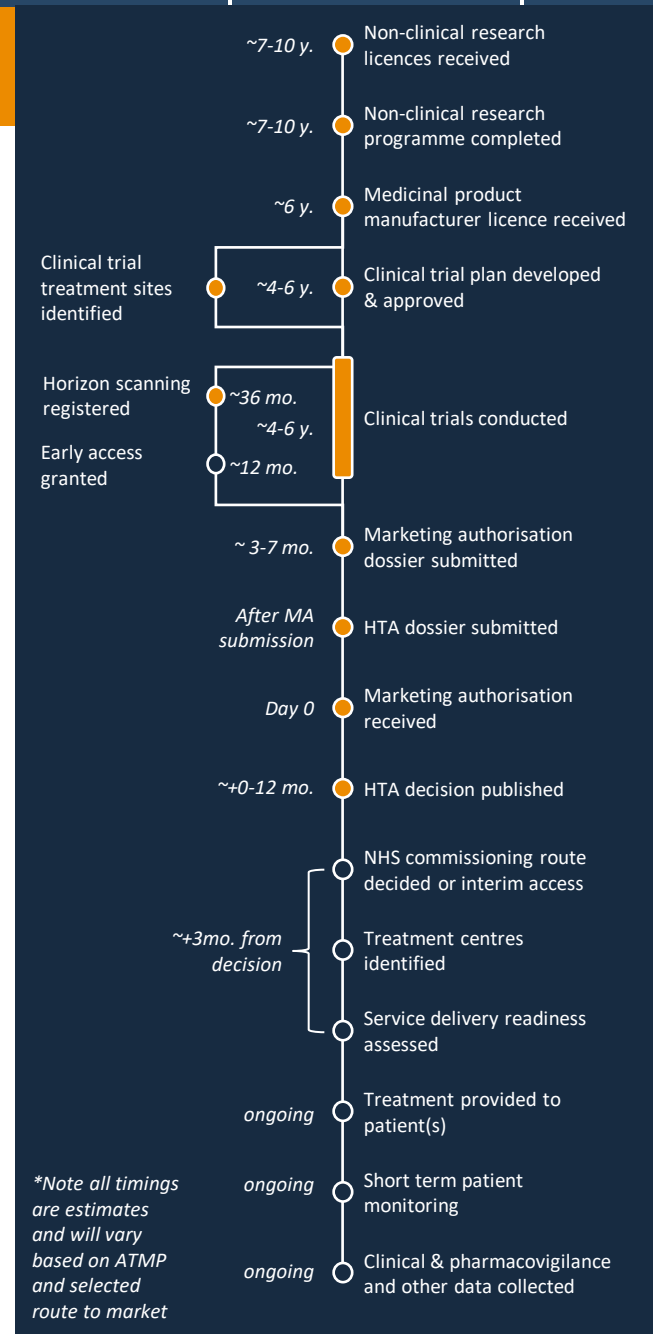
For oncology products, interim funding from the CDF (and forthcoming Innovative Medicines Fund) may be available from the point of publication of FAD, if a draft recommendation has been received (and the developer has an interim funding agreement). The interim funding ends 90 days after publication of the NICE Guidance, at which point funding switches to specialised commissioning budget*.

The statutory 90 days can be exceeded in specific circumstances, for example, where the delivery of the ATMP is particularly complex.

For an EAMS product (non-oncology or oncology), NICE will fast-track appraisals. Once NICE has reviewed and made a positive recommendation, NHS England is required to commission the service within 30 days, rather than the standard 90 days.

*Periodic re-review process will be undertaken by NICE
*Commissioning of services may change to ICS commissioning process in the future

Linked steps | Who is involved? | Best practices & tips



# 1 How are ATMPs commissioned?

## KEY TOPICS

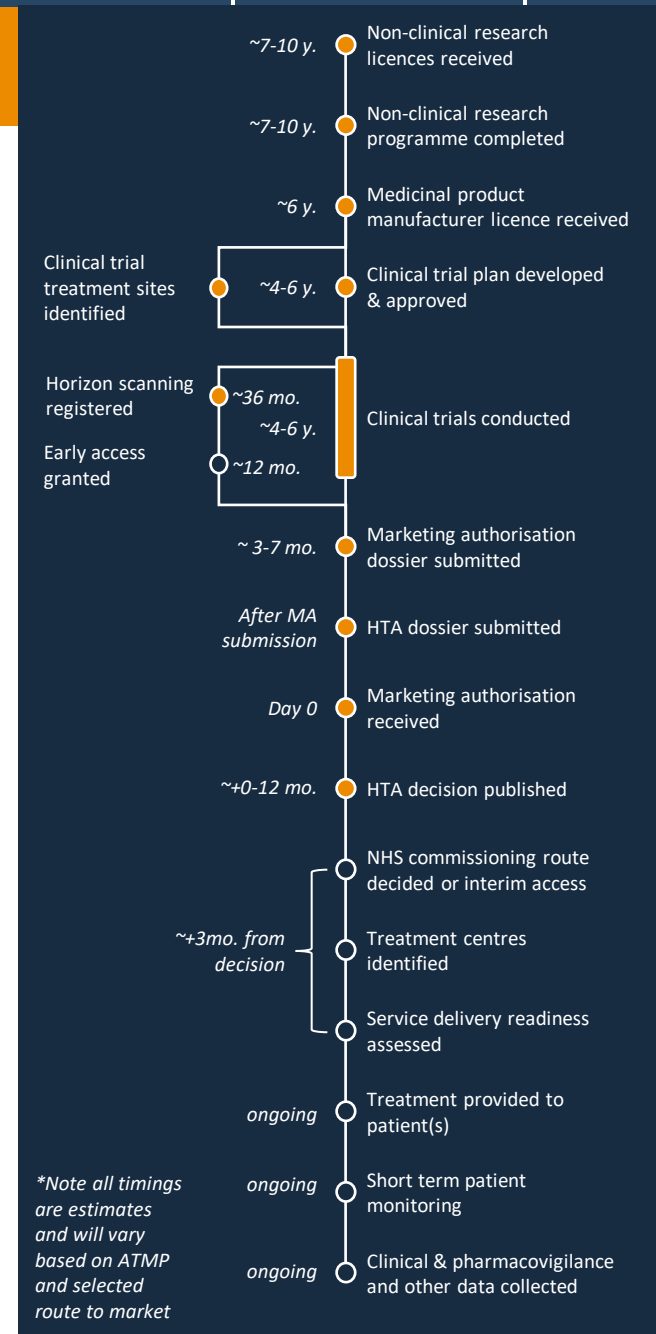
- **Routine commissioning**
- Commissioning via Managed Access

Overview | **To-do list** | Output

- Whilst commissioning decisions are ongoing, developers should plan for service delivery readiness
- NHS to ensure ATMP available within 90 days of publication of Guidance/FAD

**When**

After positive recommendation received from NICE




Linked steps | Who is involved? | Best practices & tips

# 1 How are ATMPs commissioned?

## KEY TOPICS

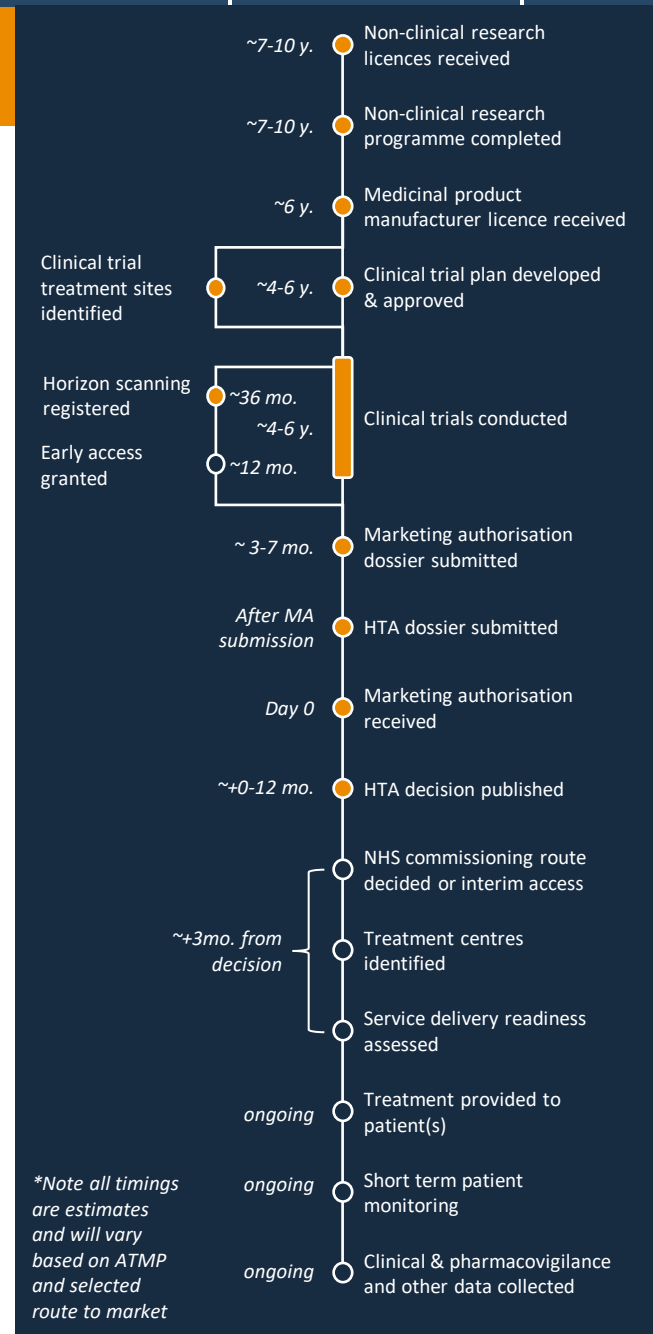
- **Routine commissioning**
- Commissioning via Managed Access

## Overview

- Funding and product availability within the NHS

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

# 1 How are ATMPs commissioned?

## KEY TOPICS

- **Routine commissioning**
- Commissioning via Managed Access

## Overview

Health Technology Assessment Technology Appraisal

Health Technology Assessment Highly Specialised Technologies evaluation

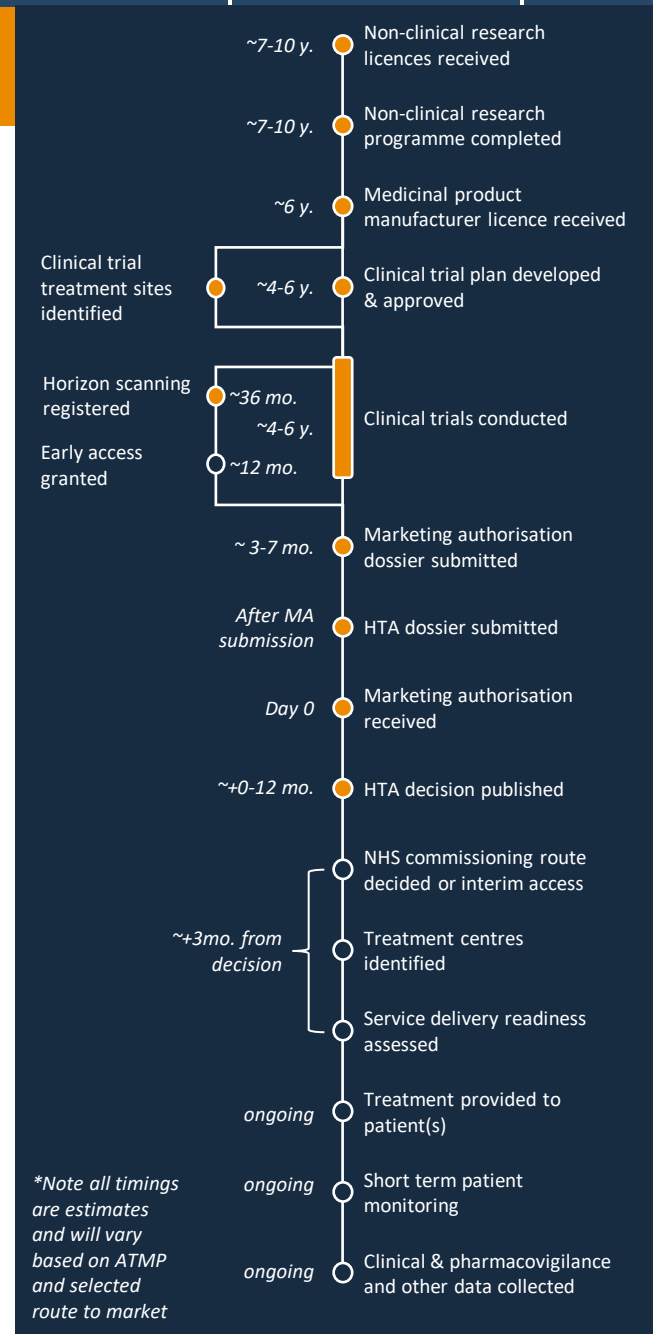
Service delivery readiness

Data collection

## To-do list

## Output

**Linked steps** **Who is involved?** **Best practices & tips**



# 1 How are ATMPs commissioned?

## KEY TOPICS

- **Routine commissioning**
- Commissioning via Managed Access

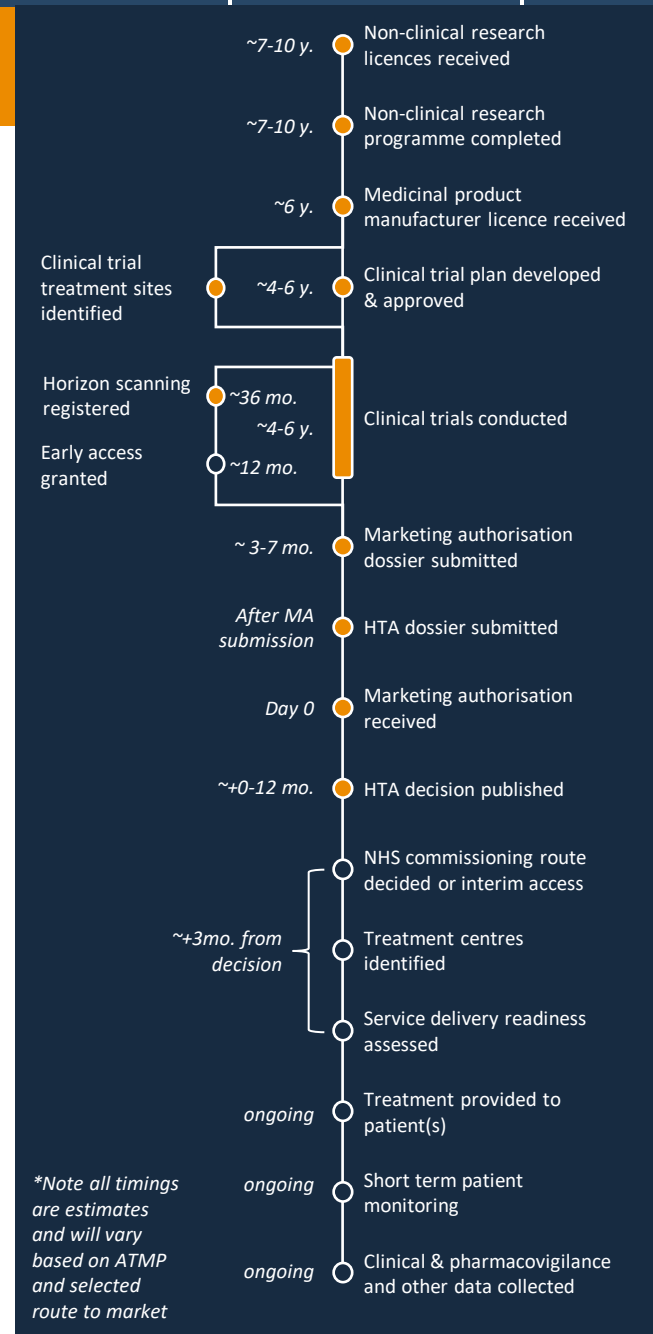
## Overview

- NICE
- NHSE

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



# 1 How are ATMPs commissioned?

## KEY TOPICS

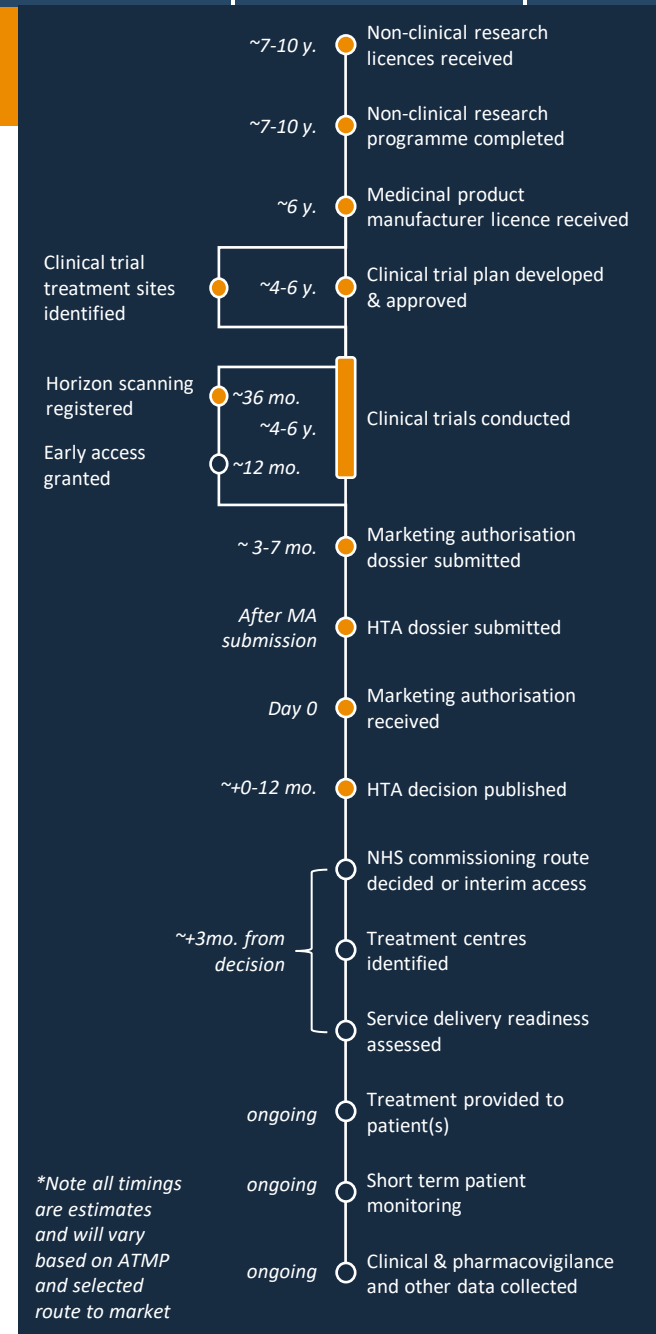
- **Routine commissioning**
- Commissioning via Managed Access

## Overview

- ATMP developers should be engaging with NHSE throughout the commissioning and implementation process, and ensure that they are planning for service delivery readiness with NHSE

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

# 1 How are ATMPs commissioned?

## KEY TOPICS

- Routine commissioning
- **Commissioning via Managed Access**

**Overview** | To-do list | Output

Once a product has been assessed by NICE TA or HST and receives a recommendation for Managed Access and a Managed Access Agreement is in place, funding becomes available 90 days after the NICE guidance is issued.

For an oncology product that have been has been assessed by NICE TA or HST and receives a recommendation for Managed Access and a Managed Access Agreement via CDF is in place, funding will be provided through CDF and the treatment may be available earlier. Note that MAA are also expected to be used with the forthcoming Innovative Medicines Fund (IMF).

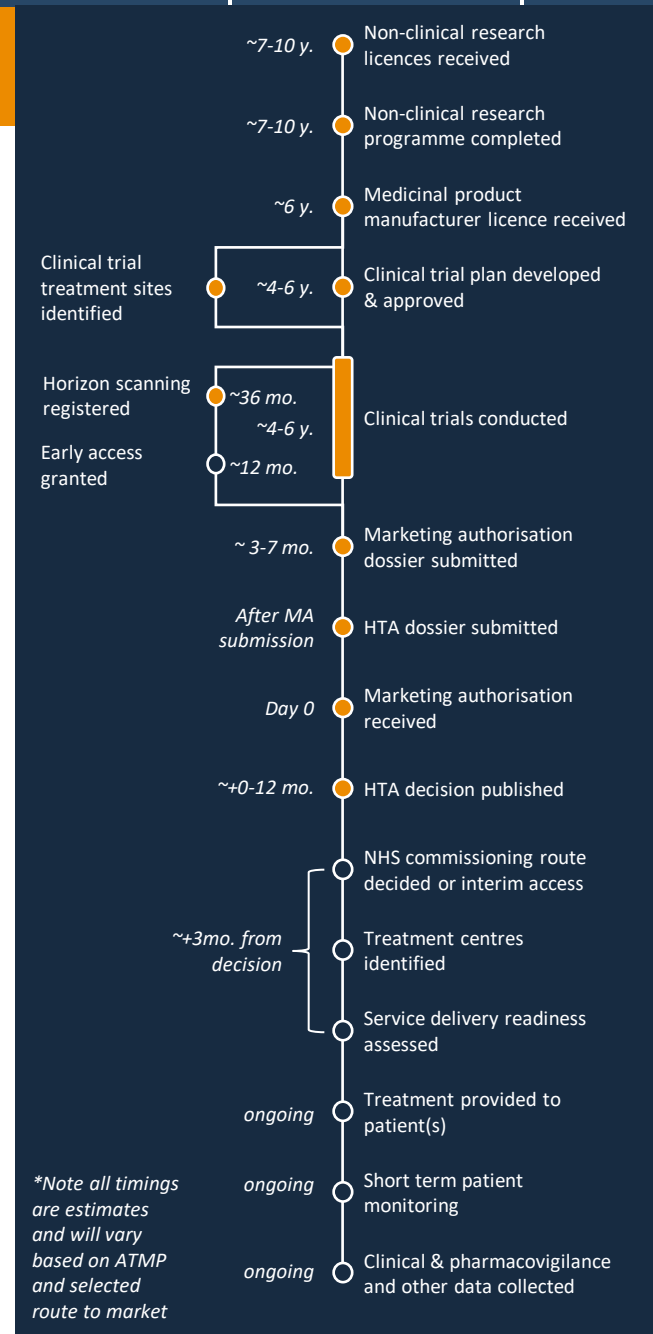
Developers must then ensure that data are collected as per the Data Collection Agreement within the Managed Access Agreement. The ATMP will exit managed access (including the CDF) at an agreed point in time, which will be specified in the Data Collection Agreement.

NICE will then schedule a re-evaluation & take account of new data available and (if applicable) newly proposed price.

- If a positive recommendation is received the funding will switch from CDF to routine commissioning*
- If a product is not recommended for routine commissioning, then there are no further options for commissioning (except via Individual Funding Request under highly exceptional circumstances)

* Commissioning of services may change to ICS commissioning process in the future

Linked steps | Who is involved? | Best practices & tips



# 1 How are ATMPs commissioned?

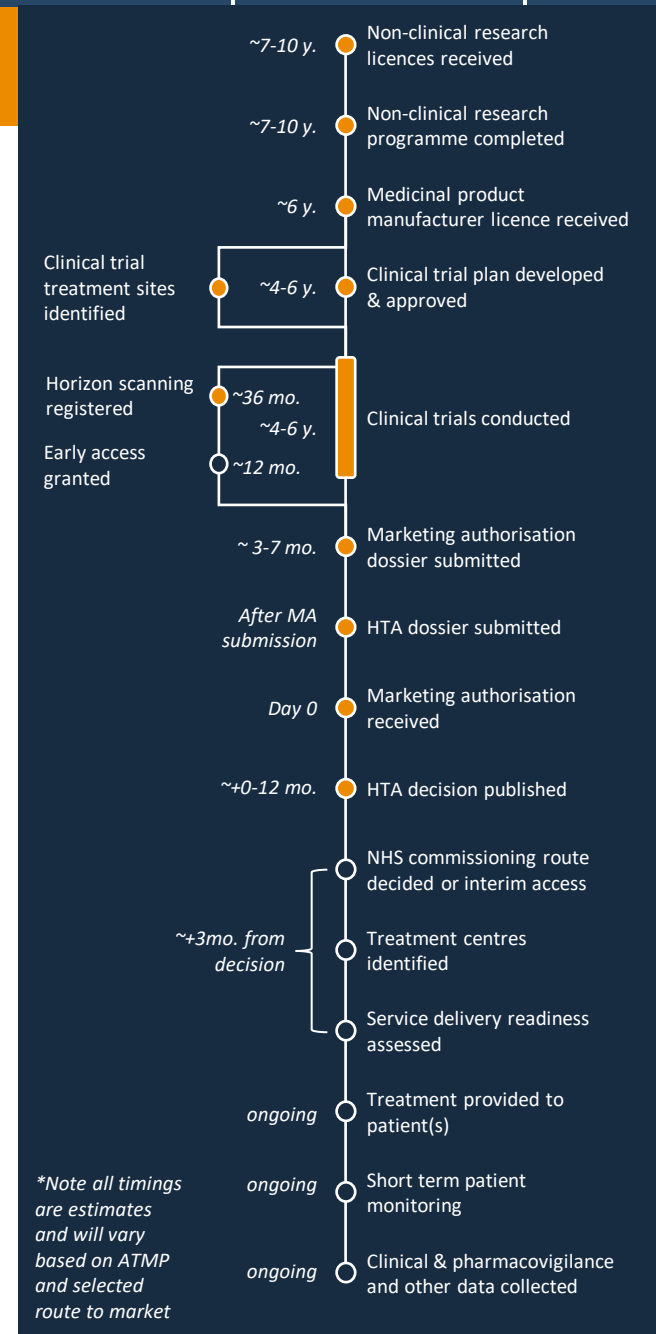
## KEY TOPICS

- Routine commissioning
- **Commissioning via Managed Access**

Overview | **To-do list** | Output

- Engage with NICE on potential and feasibility for Real World Data collection to address evidential uncertainties
- Whilst commissioning decisions are ongoing, both developers and NHS should plan for service delivery readiness
- NHS to ensure ATMP available within 90 days of NICE Guidance

**When**
After a Managed Access recommendation is received from NICE




Linked steps | Who is involved? | Best practices & tips

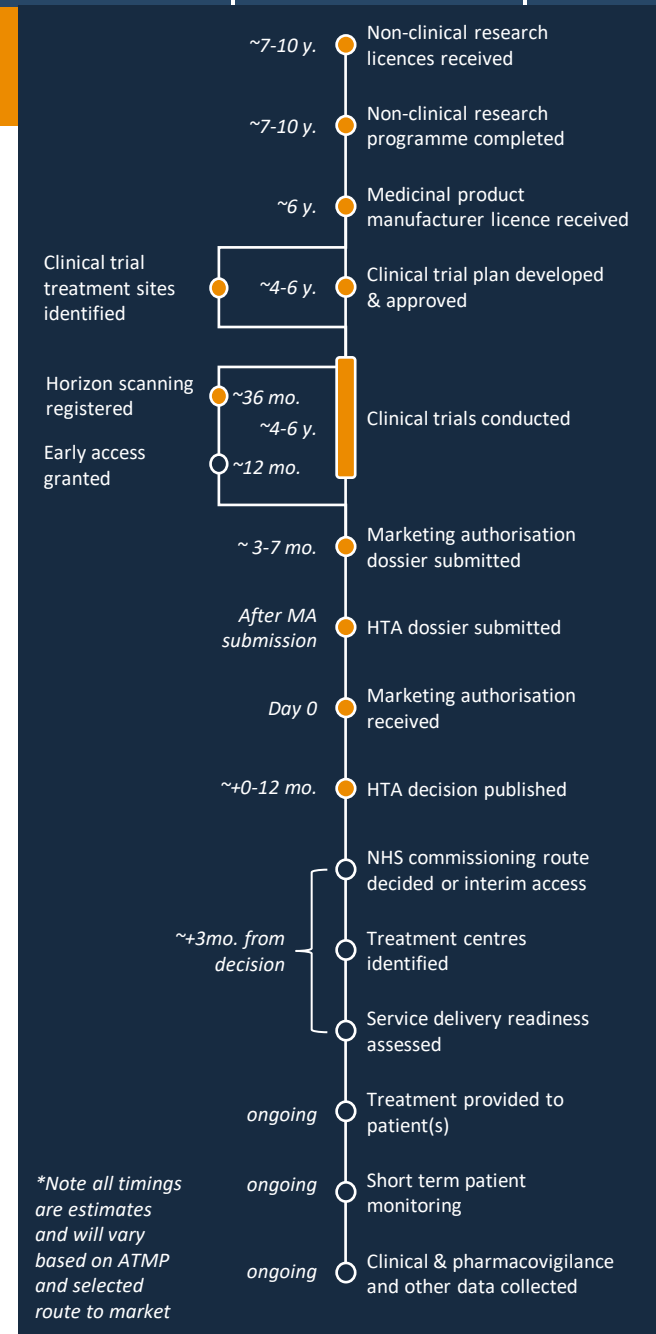
# 1 How are ATMPs commissioned?

## KEY TOPICS

- Routine commissioning
- **Commissioning via Managed Access**

Overview | To-do list | **Output**

- Funding and product availability within the NHS




Linked steps | Who is involved? | Best practices & tips

# 1 How are ATMPs commissioned?

## KEY TOPICS

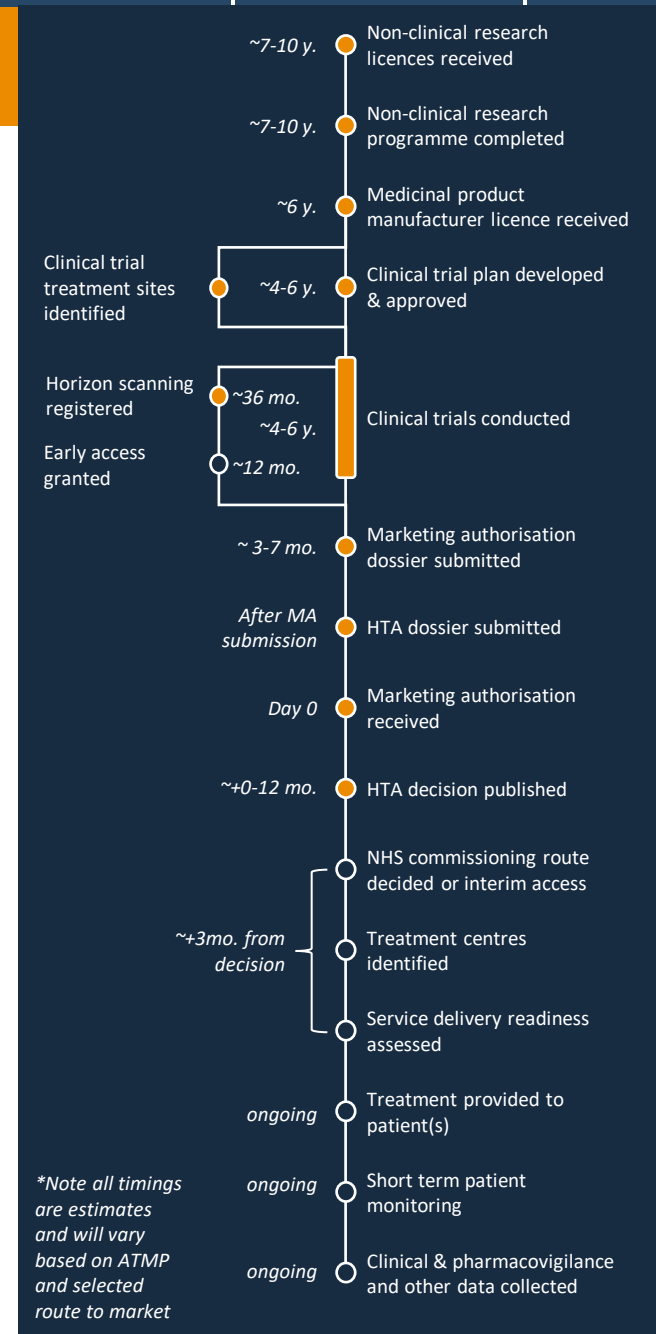
- Routine commissioning
- **Commissioning via Managed Access**

## Overview

- Health Technology Assessment Technology Appraisal
- Health Technology Assessment Highly Specialised Technologies evaluation
- Managed Access Agreement [optional]
- Service delivery readiness
- Data collection

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips

# 1 How are ATMPs commissioned?

## KEY TOPICS

- Routine commissioning
- **Commissioning via Managed Access**

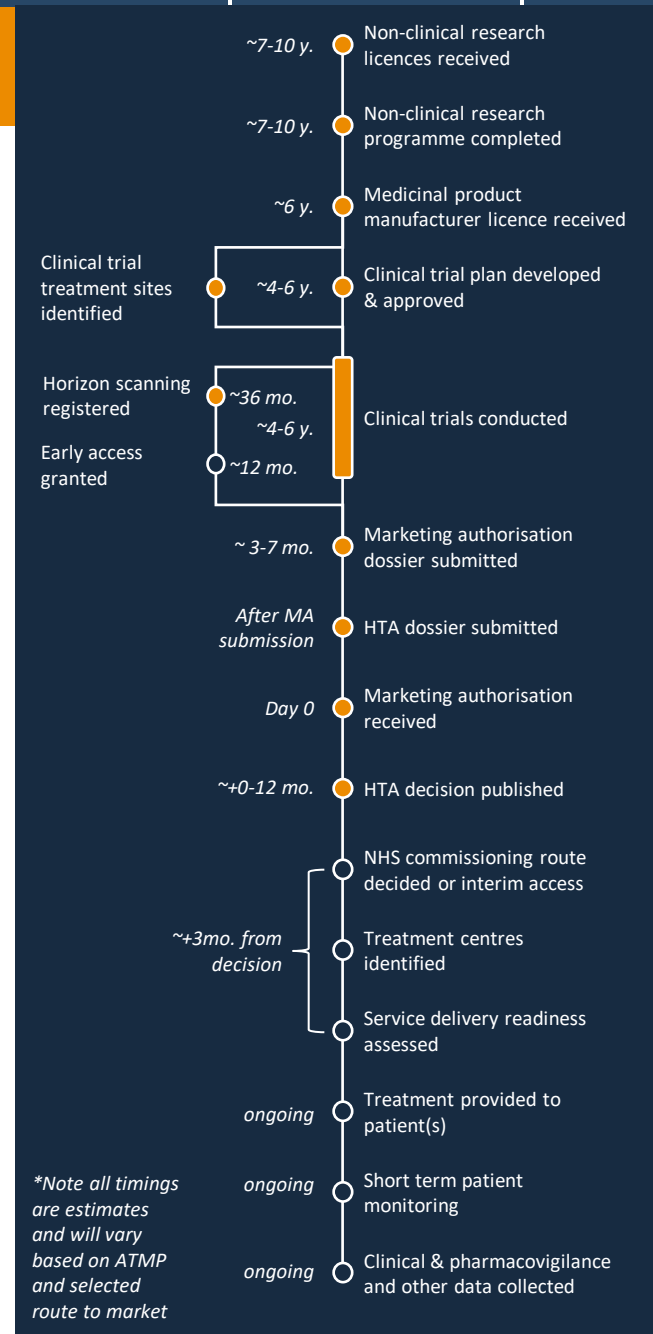
## Overview

- NICE
- NHSE
- Relevant Data Controller e.g. a registry

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



# 1 How are ATMPs commissioned?

## KEY TOPICS

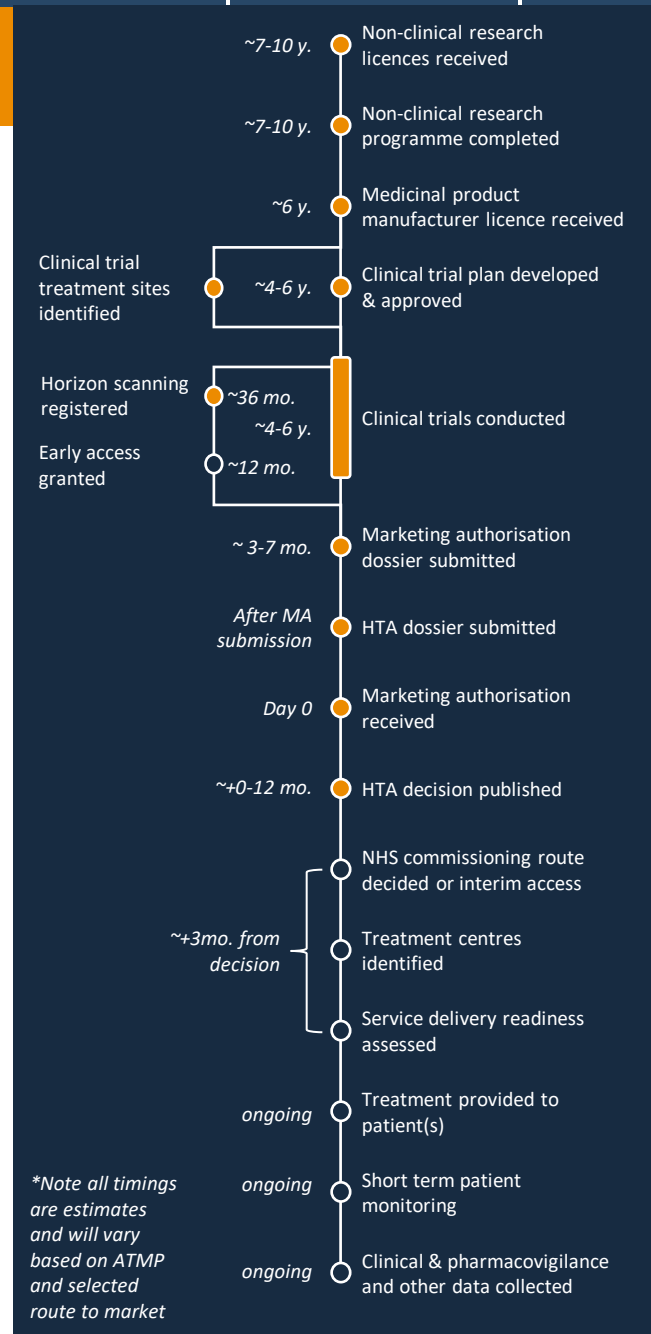
- Routine commissioning
- **Commissioning via Managed Access**

## Overview

## To-do list

## Output

- If the ATMP product is a long term therapy, developers should consider exit criteria and funding/provision of treatments for existing patients in the event of a negative NICE decision on re-evaluation




Linked steps | Who is involved? | Best practices & tips

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

- **Service delivery readiness**
- Treatment centre identification

**Overview** | To-do list | Output

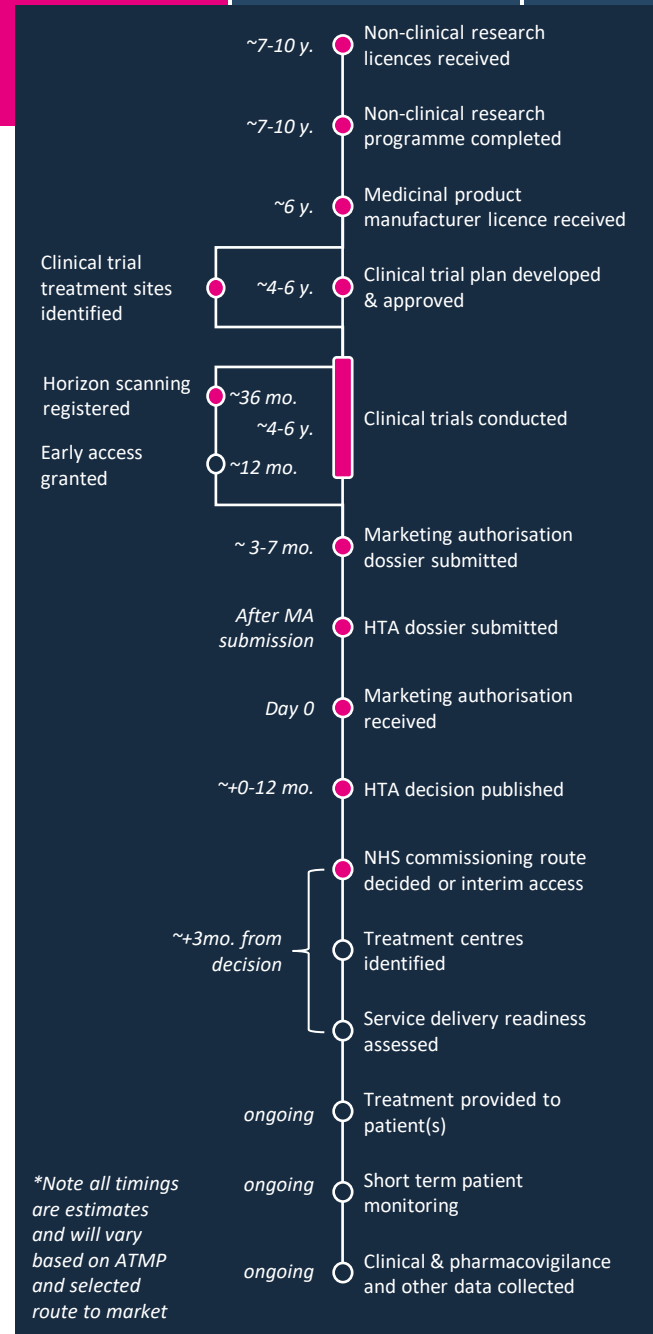
NHS commissioned and clinical trial treatment centres and developers should review the relevant service specification for ATMP (if applicable) and review the ATTC NHS readiness toolkit to prepare for the delivery of ATMPs

Developers should engage with treatment centre(s) selected by NHSE as part of the commissioning process to support them in preparation for ATMP treatment provision once the commissioning decision has been communicated.

When considering service delivery for clinical trials, developers should engage with treatment centre(s) where they are planning to conduct the clinical trials to ensure that they have the relevant capabilities and are sufficiently prepared.

Organisations must have in place a strategic plan regarding the use of ATMPs and a governance process to introduce them safely. This should be led by the Chief Pharmacist and should enable governance operational and clinical considerations to be highlighted.

Linked steps | Who is involved? | Best practices & tips



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

- **Service delivery readiness**
- Treatment centre identification

Overview | **To-do list** | Output

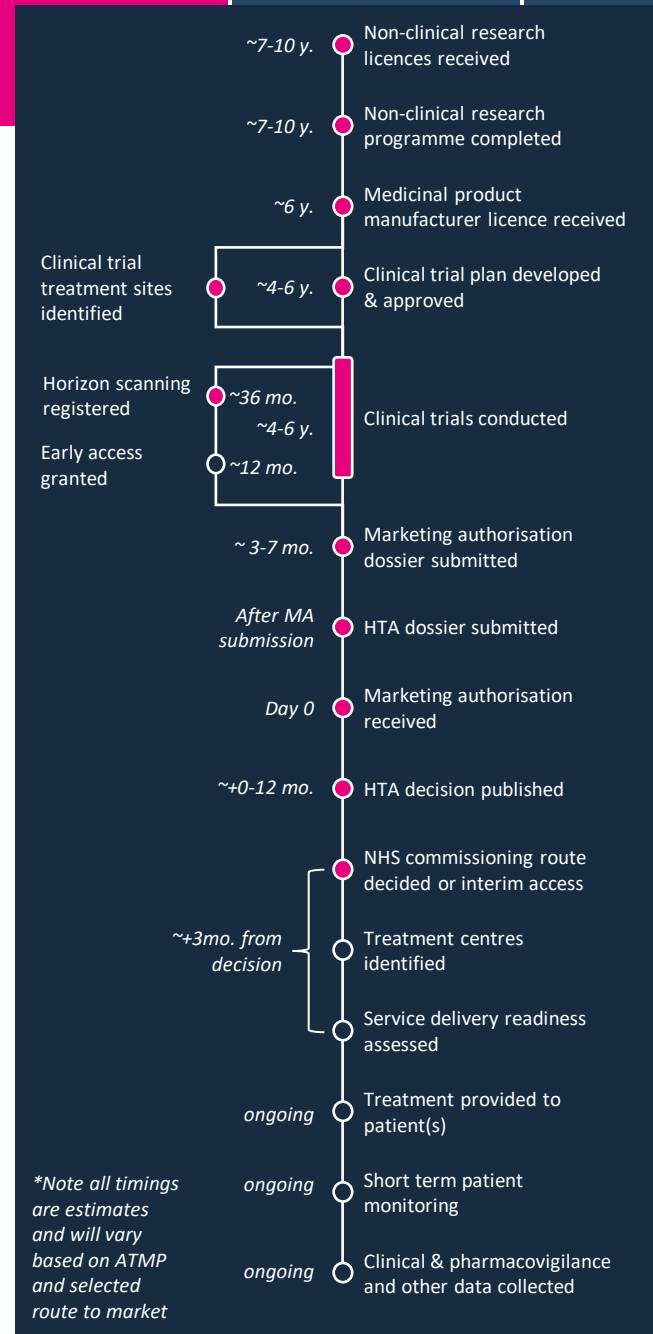
- Review the full ATTC readiness toolkit here
  - Guidance and resources related to governance can be found here
  - Guidance and resources related to business and financial planning can be found here
  - Guidance and resources related to quality assurance and risk assessments can be found here
  - Guidance and resources related to operational delivery and in-hospital logistic requirements can be found here
  - Guidance and resources related to clinical practice can be found here
  - Guidance and resources related to education and training of staff can be found here
  - Guidance and resources related to long term follow-up of patients can be found here
- Review the SPS QA advice document here

**When**

Remaining service delivery readiness steps completed after access recommendation received from NICE

- [Service delivery for clinical trials] During clinical trial planning and design

**Linked steps** | **Who is involved?** | **Best practices & tips**



# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

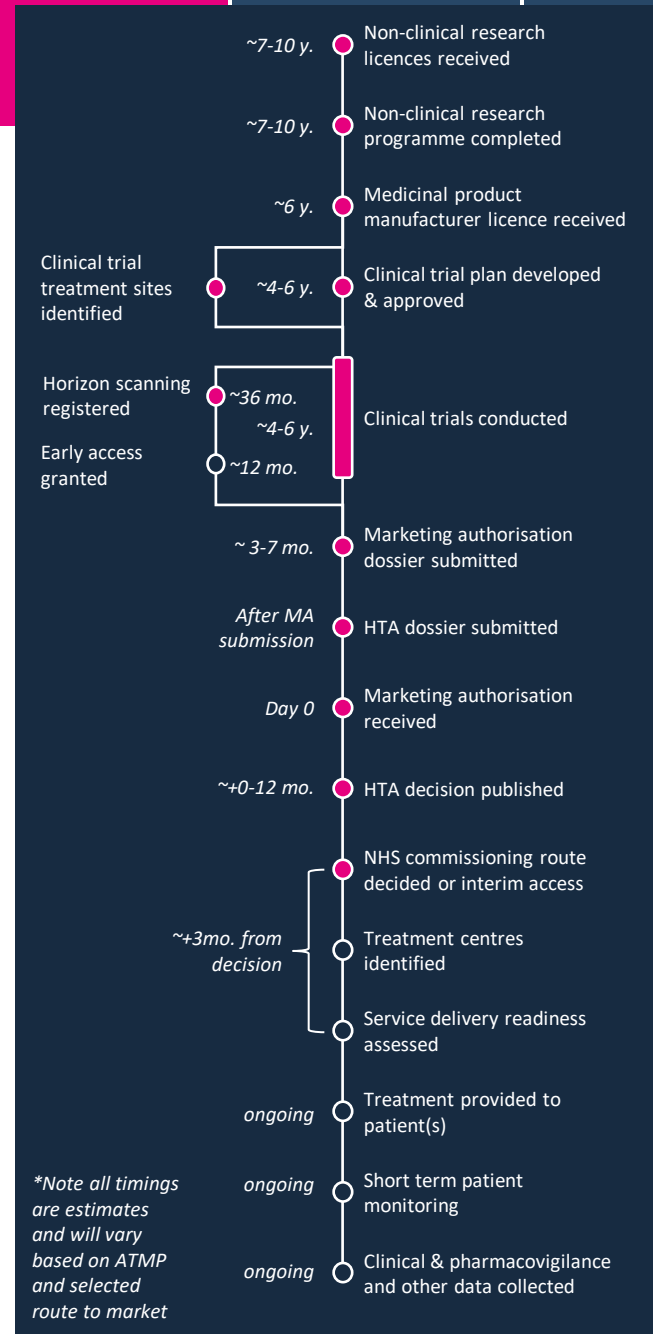
**Service delivery readiness**

Treatment centre identification

Overview | To-do list | **Output**

- Services in place to support ATMP delivery within NHS
- [Service delivery for clinical trials] NHS treatment centre readiness for conducting clinical trial(s)

**Linked steps** | **Who is involved?** | **Best practices & tips**



# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

- **Service delivery readiness**
- Treatment centre identification

## Overview

Clinical trial planning, design & protocol development

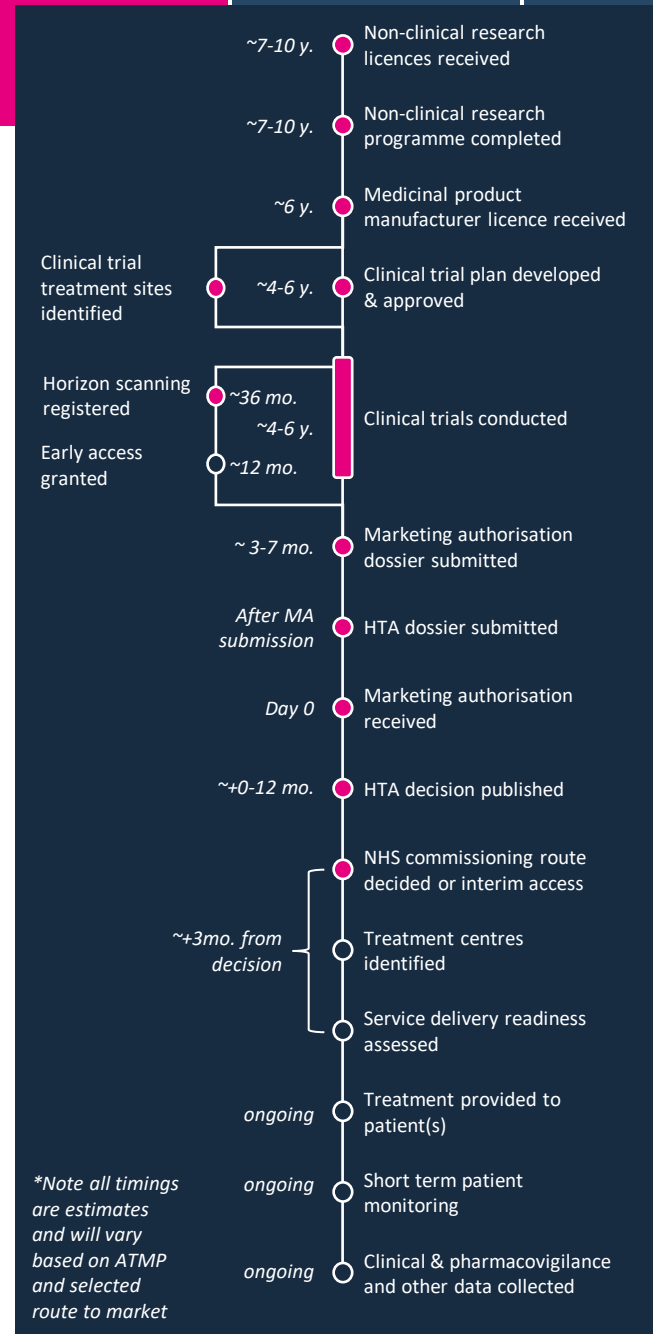
Routine commissioning

Commissioning via Managed Access

**Linked steps** **Who is involved?** **Best practices & tips**

## To-do list

## Output



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

- **Service delivery readiness**
- Treatment centre identification

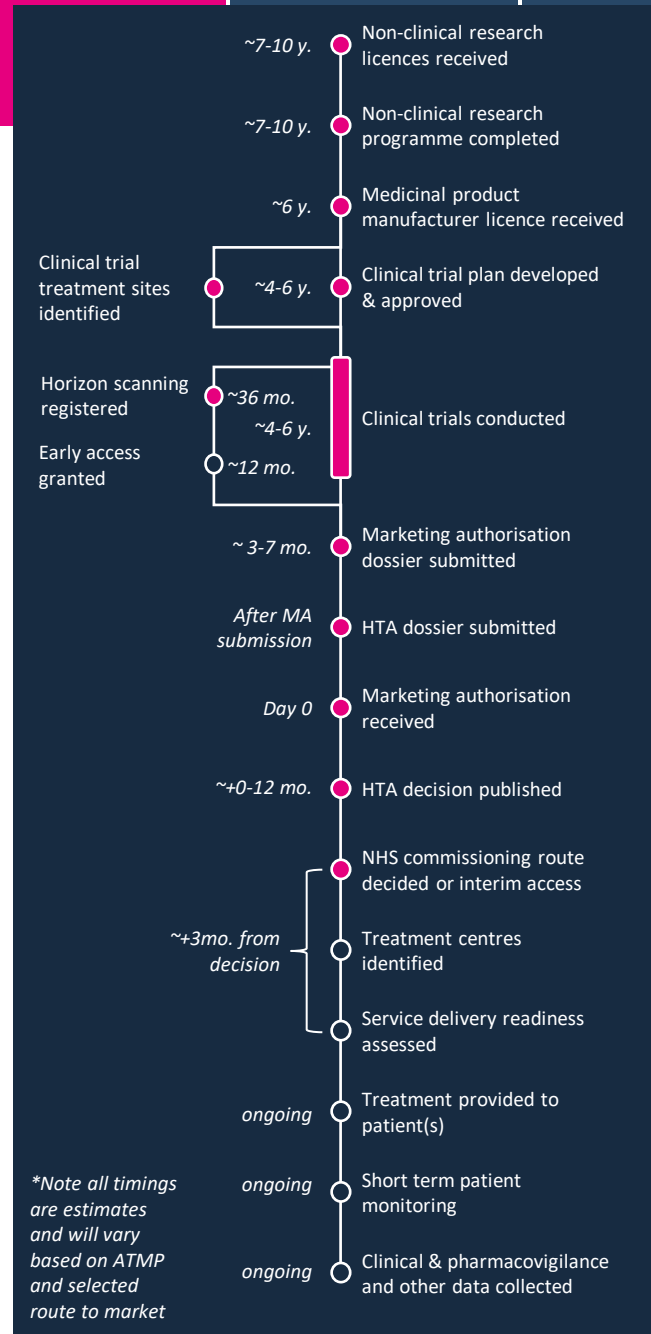
## Overview

- ATMP developer
- NHSE
- NHS ATMP treatment centres

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

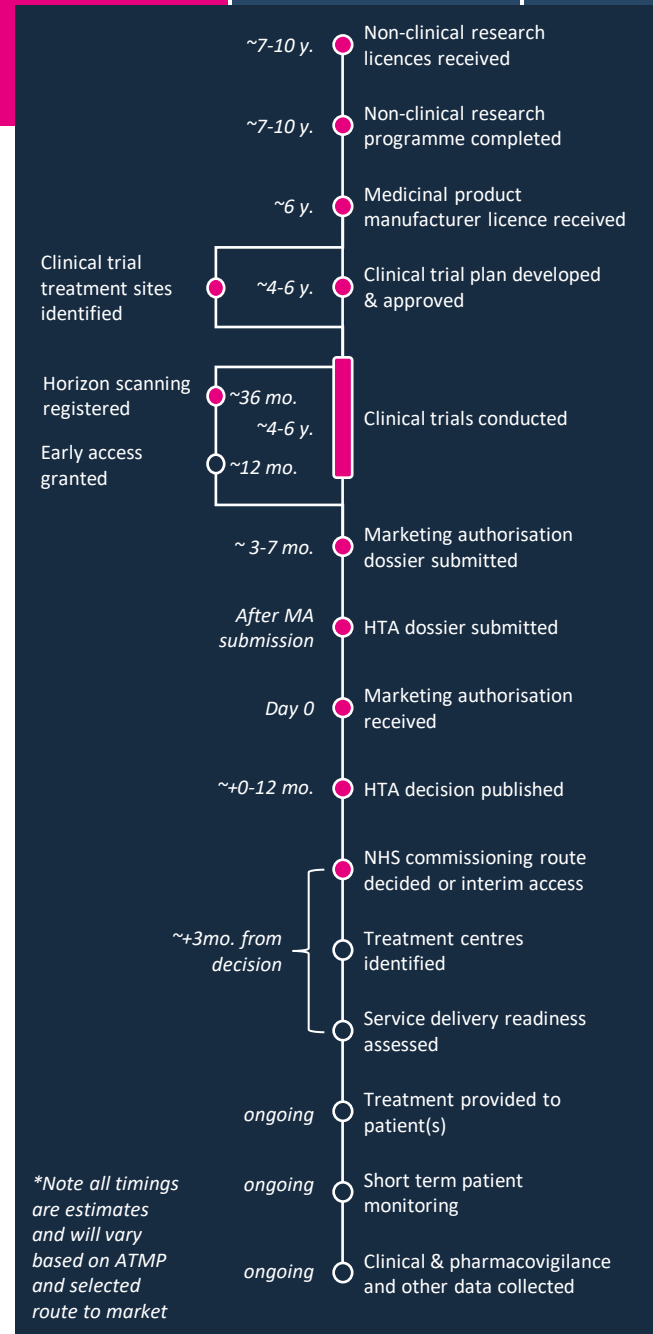
- **Service delivery readiness**
- Treatment centre identification

## Overview

- Awareness of service delivery readiness requirements will help developers shape approach for engaging with NICE and NHSE before/during HTA
- Developers should also review guidance from the NHS Specialist Pharmacy Service here, which highlights implementation challenges faced by the NHS and suggests design considerations to minimise them
- Where a MA holder anticipates a direct contract being required for each delivery centre early development of the contract and sharing with sites (via Pan UK Pharmacy Working Group for ATMPs) for a collaborative review can reduce delay in implementation post commissioning

## To-do list

## Output




**Linked steps** | **Who is involved?** | **Best practices & tips**

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

- Service delivery readiness
- **Treatment centre identification**

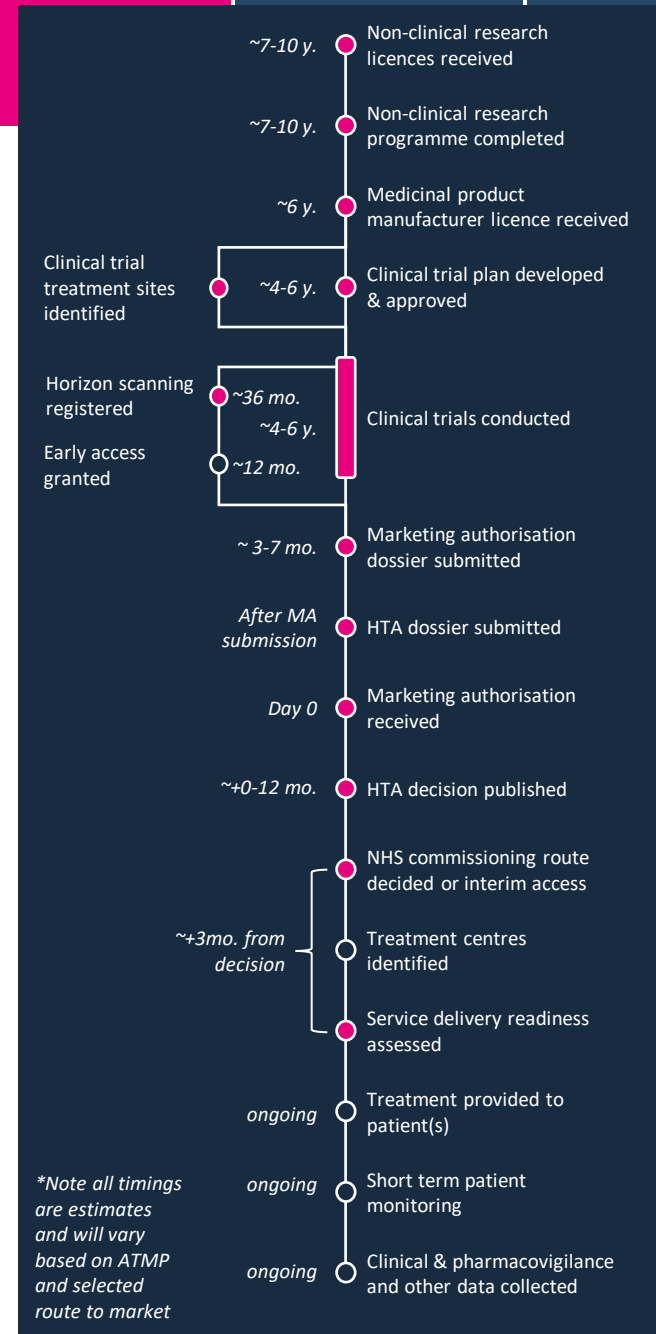
**Overview** | To-do list | Output

For commissioned products, NHSE select the number of and specific treatment centres to deliver ATMPs (this will depend on expected number patients, capability of centres etc.) as part of their commissioning decision after NICE recommend reimbursement.

NHSE will confirm that treatment centres:

- Have accreditation from relevant body if required (e.g. JACIE for cell & ex-vivo gene therapies, HTA for cell & tissue)
- Have appropriate governance approvals in place

NHSE will then cascade treatment centre decision down to regional and local treatment centres for confirmation they wish to be involved. Developers can then engage with treatment centres to get service up and running (this process will vary depending on the type of ATMP).




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

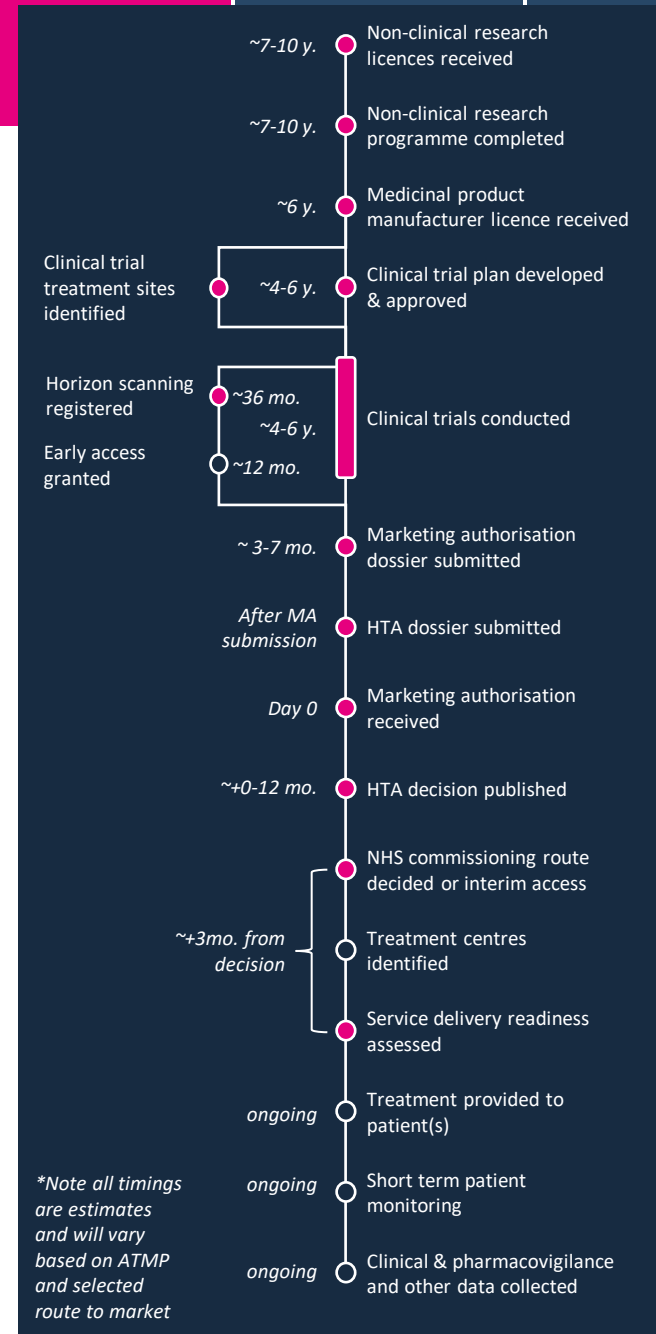
- Service delivery readiness
- **Treatment centre identification**

Overview | **To-do list** | Output

- Engage with NHS treatment centres once decision received from NHSE

**When**

- After positive recommendation received from NICE




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

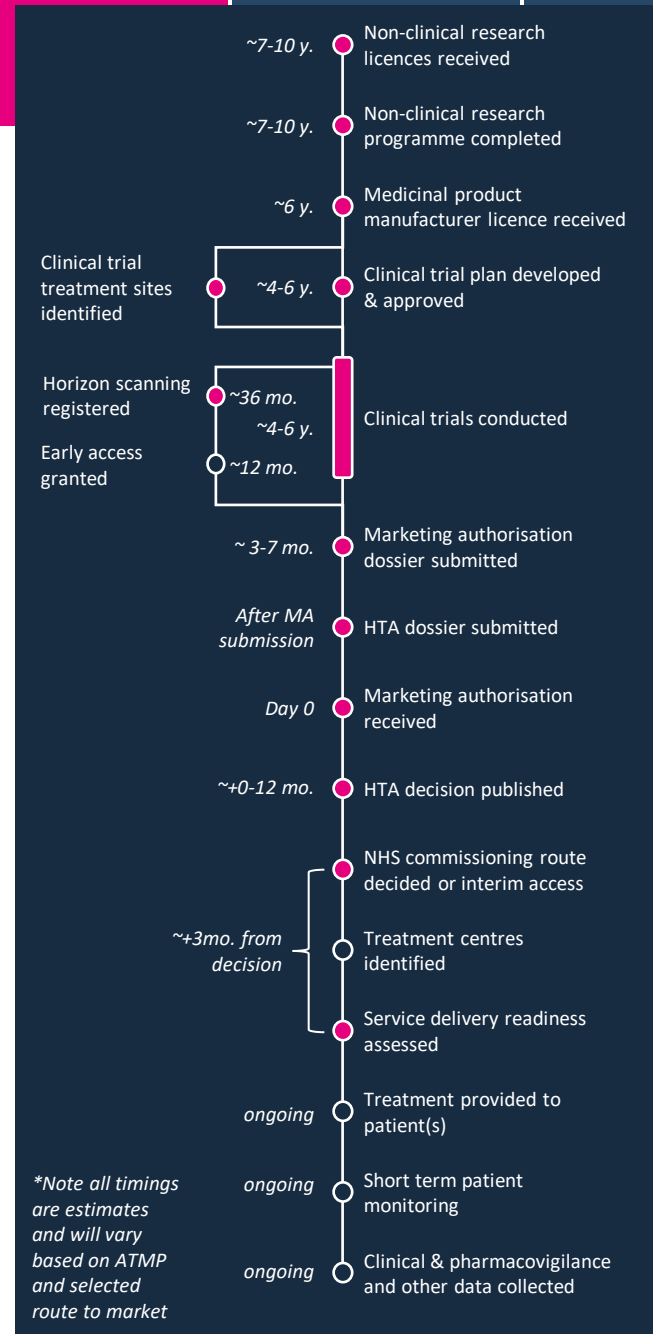
- Service delivery readiness
- **Treatment centre identification**

## Overview

- Treatment centres identified for ATMP provision

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

- Service delivery readiness
- **Treatment centre identification**

## Overview

## To-do list

## Output

Routine commissioning

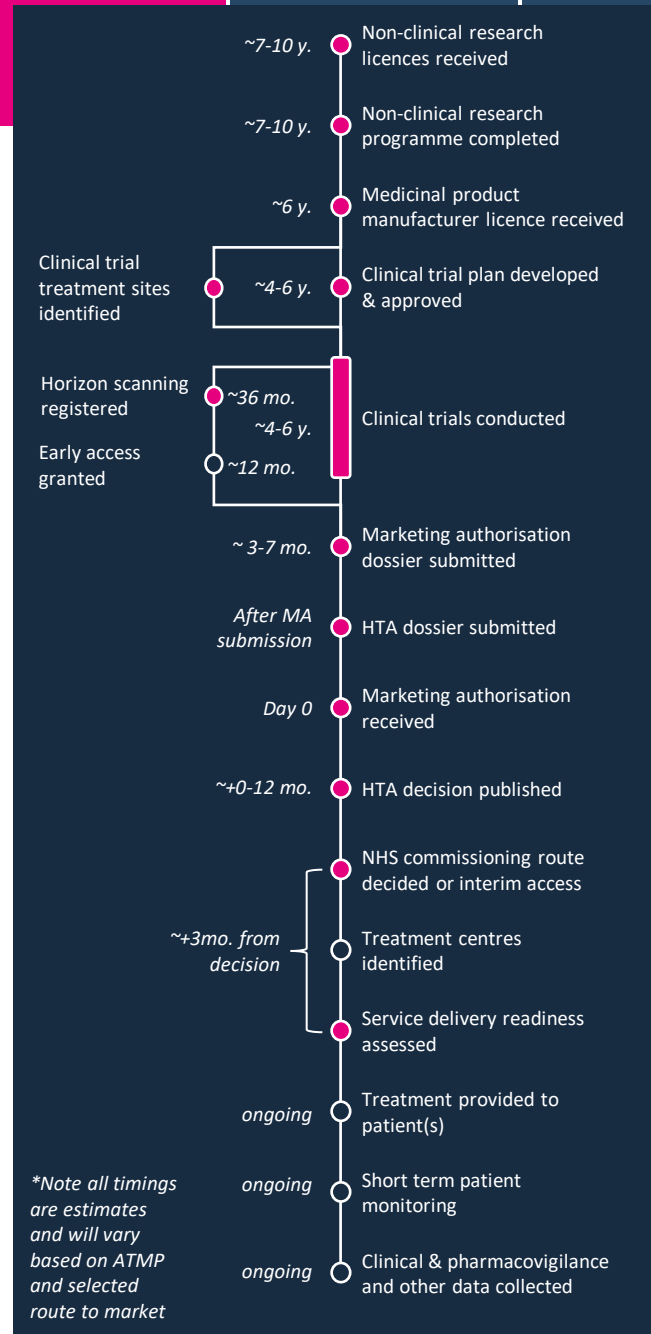
Commissioning via Managed Access

**Linked steps**

**Who is involved?**

**Best practices & tips**

**Variation by devolved nation**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

- Service delivery readiness
- **Treatment centre identification**

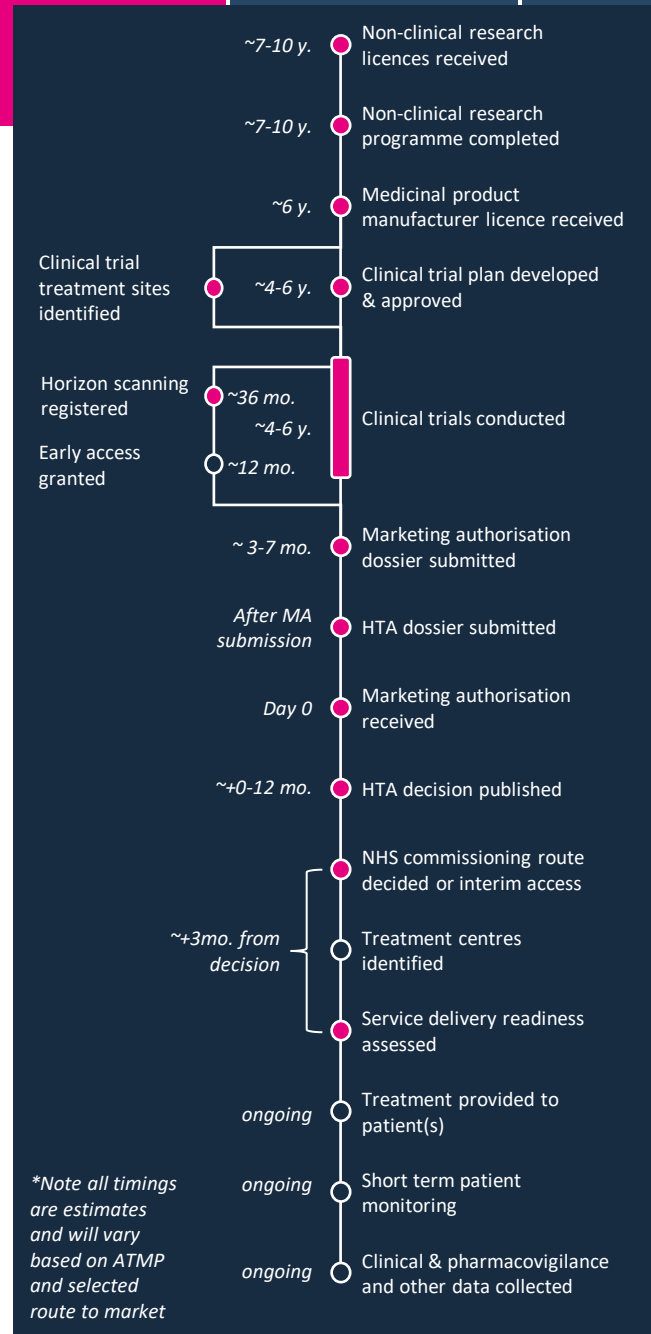
## Overview

- ATMP developer
- NHSE
- Regional and local hospital management teams

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips** | **Variation by devolved nation**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

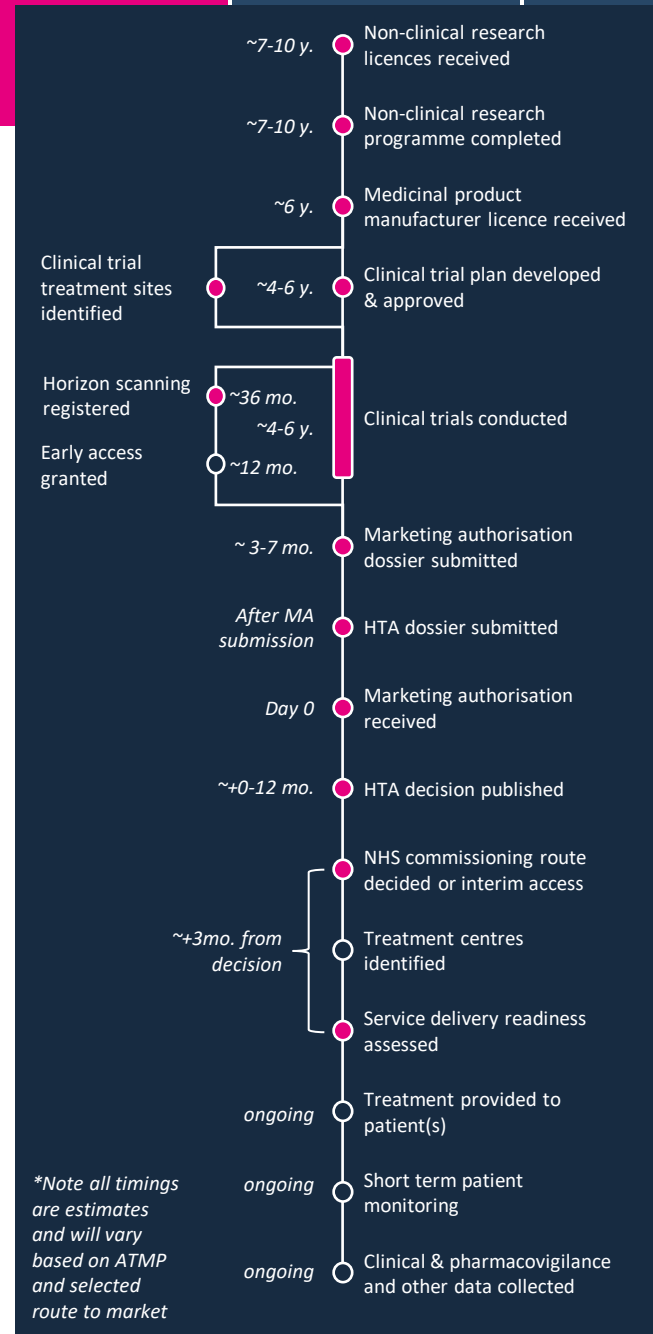
- Service delivery readiness
- **Treatment centre identification**

## Overview

- For some new specialised ATMPs, it may be challenging for NHS treatment centres to prepare for provision within the 90 day time limit provided. It is therefore advisable for Developers to engage with treatment centres as early as possible, however there will be limits on the scope of preparations that can be done prior to official confirmation from NICE that the product will be recommended.
- Developers should engage early with NHSE to support development of a service specification if required
- Developers are recommended to collect data on the cost of provision (including on-site storage, preparation, administration etc) for their ATMP within the NHS to help inform delivery tariffs if these are significant

## To-do list

## Output




Linked steps | Who is involved? | Best practices & tips | Variation by devolved nation

# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

**Treatment centre identification (Wales)**

Overview | To-do list | Output

For commissioned products, Welsh Health Specialised Services Committee (WHSSC) select the treatment centres on behalf of the Health Boards to deliver ATMPs. WHSSC commissions ATMPs that are approved by the NICE process as NICE approvals are mandated for Wales, subject to Ministerial approval. AWMSG provide horizon scanning information to WHSSC to inform planning of future capacity requirements for WHSSC to commission.

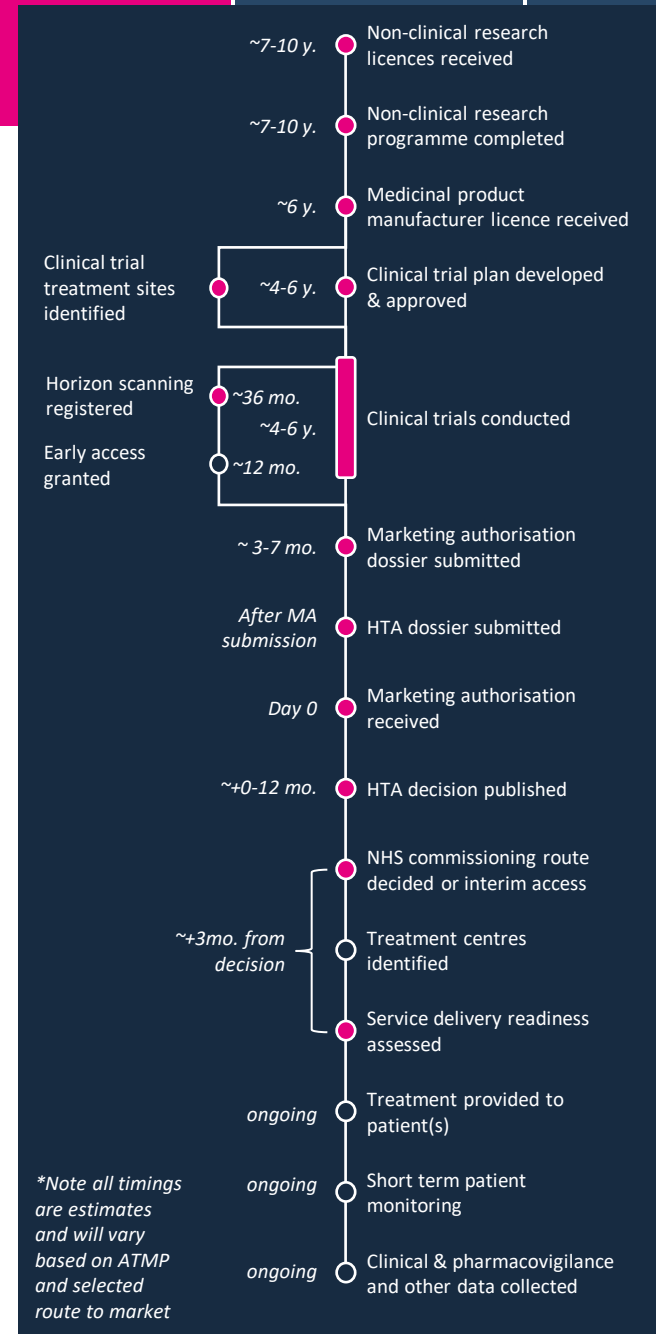
WHSSC will confirm that treatment centres:

- Have accreditation from relevant body if required (e.g. JACIE for cell & ex-vivo gene therapies, HTA for cell & tissue)
- Governance approvals in place – including accreditation from NHS England for English centres

WHSSC cascade treatment centre decision down to Health Boards and regional and local treatment centres (if applicable). Once agreed, developers can engage with treatment centres to get service up and running. The WHSSC strategic intent for ATMPs is to establish delivery centres in Wales where it is safe and appropriate to do so, taking into account the specific clinical expertise required and critical mass criteria. WHSSC will continue to commission provision from English centres which are designated by NHS England for the particular indication, where established regional cross border relationships exist and where there are small numbers of nationally designated centres for rare diseases.
Note that WHSSC may also decide to provide the treatment through Specialist Services UK, whereby Welsh patients are funded for treatment in England through a service agreement

For clinical trials, treatment centre identification is determined by the developer and may be driven by the expertise or reputation of a particular centre or physician working in the disease area.

Linked steps | Who is involved? | Best practices & tips | Back to England



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

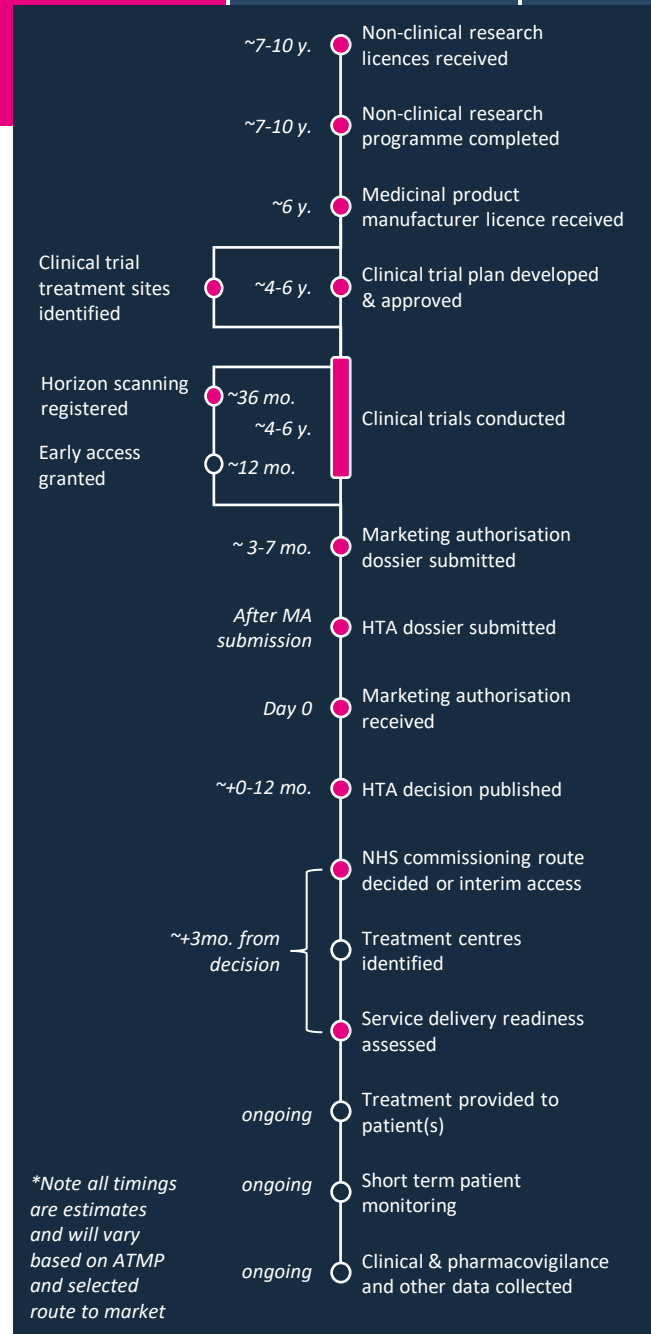
**Treatment centre identification (Wales)**

Overview | **To-do list** | Output

- Engage with NHS Wales health boards (treatment centres) once decision received from WHSSC

**When**

- After positive recommendation received from AWMSG




Linked steps | Who is involved? | Best practices & tips | Back to England

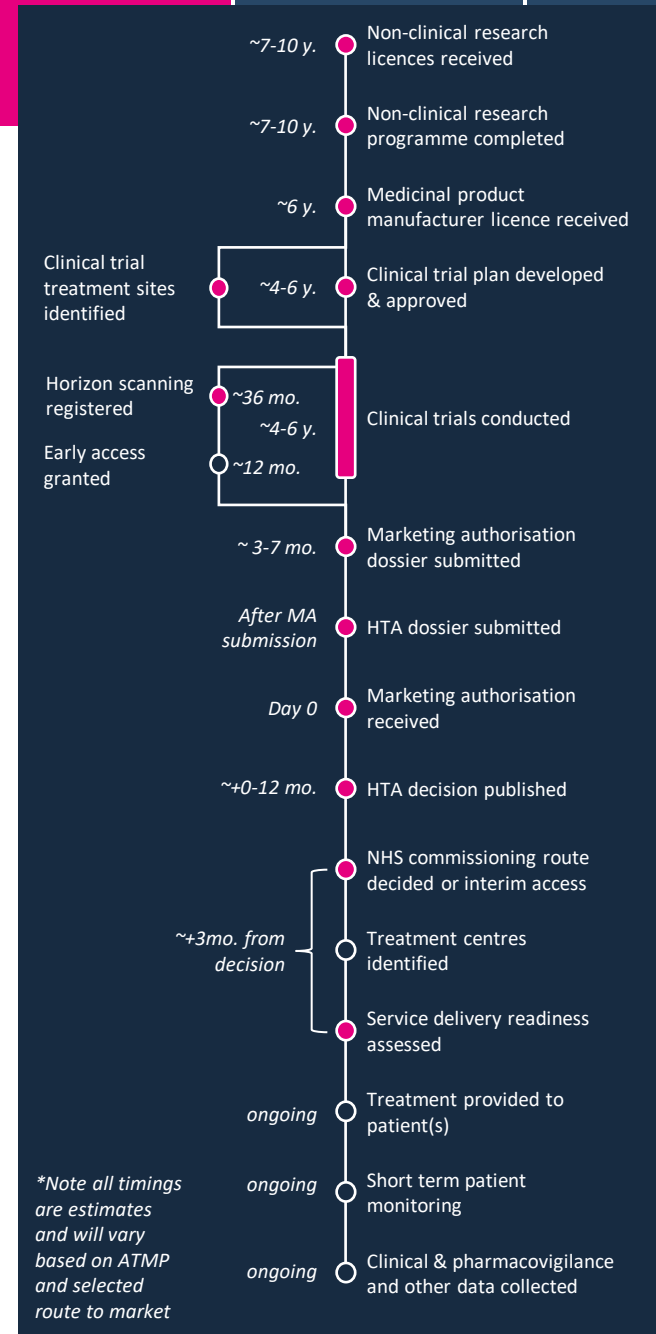
# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

**Treatment centre identification (Wales)**

Overview | To-do list | **Output**

- Treatment centres identified for ATMP provision



# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

**Treatment centre identification (Wales)**

Overview

To-do list

Output

Routine commissioning

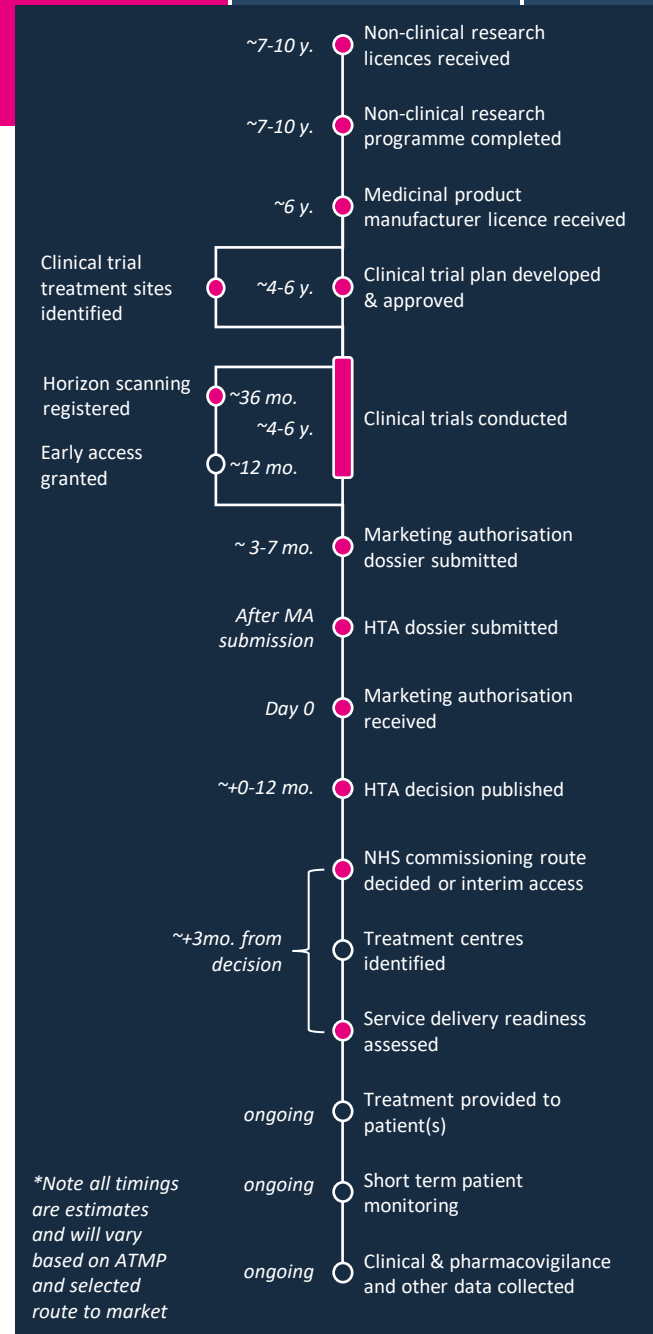
Commissioning via Managed Access

Linked steps

Who is involved?

Best practices & tips

Back to England



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

**Treatment centre identification (Wales)**

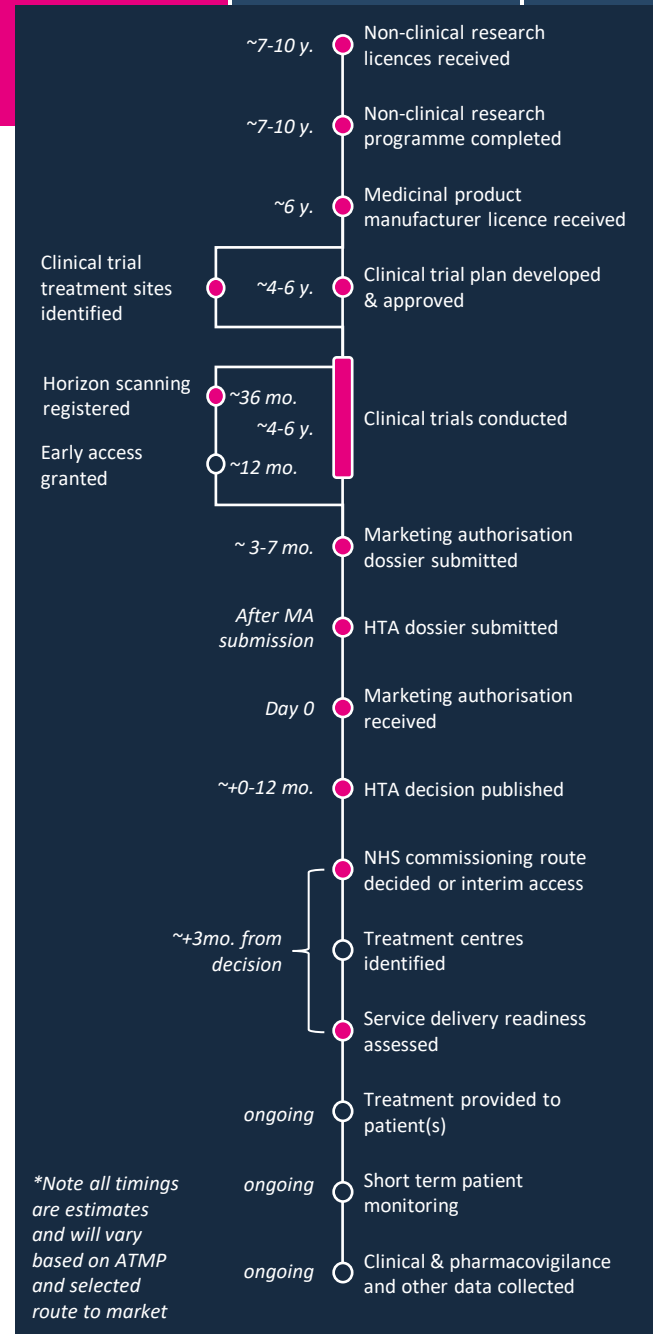
## Overview

## To-do list

- WHSSC
- ATMP developer

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips** | **Back to England**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

**Treatment centre identification (Wales)**

Overview

To-do list

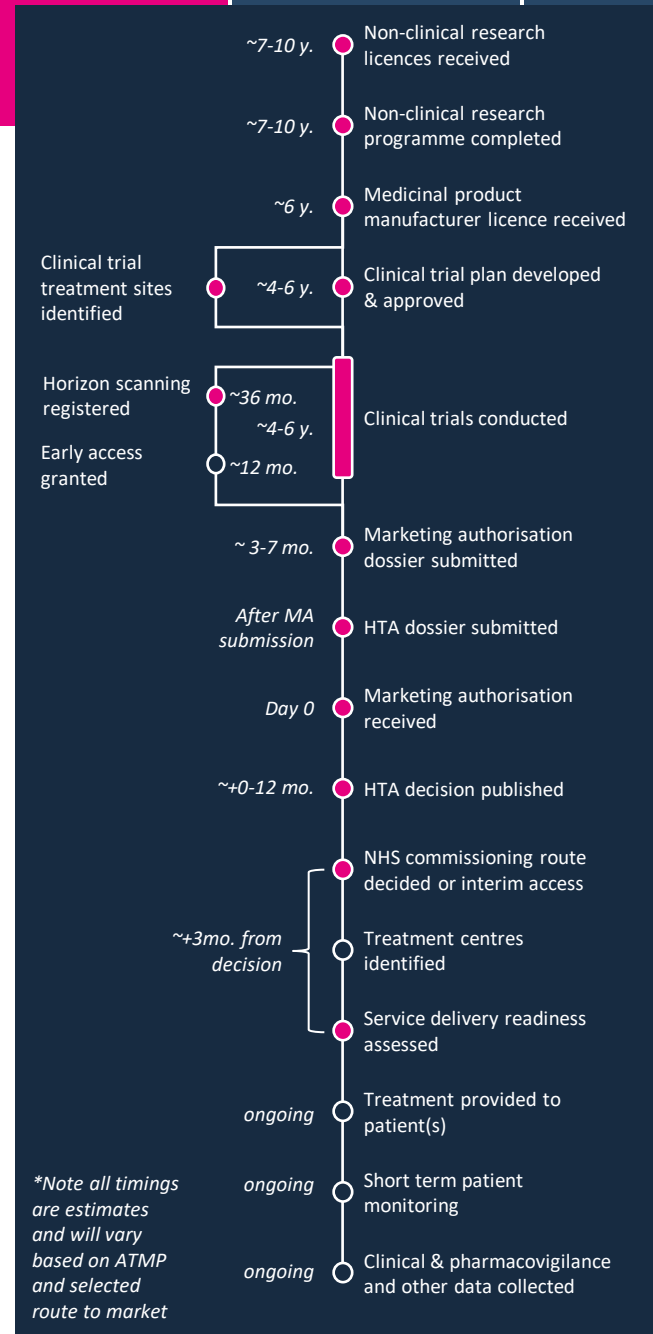
Output

**Linked steps**

**Who is involved?**

**Best practices & tips**

**Back to England**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

**Treatment centre identification (Scotland)**

Overview | To-do list | Output

For commissioned products, NHS Scotland's National Services Division runs a national designation process to identify if a specialist service is required. Services are commissioned at a national level from identified key treatment centre(s) after the SMC recommends reimbursement.
If applicable, NSS will engage the relevant National Clinical Network (or Cancer Network), or a new National Network may be commissioned*.

National Services Scotland (NSS) will confirm that treatment centres:

- Have accreditation from relevant body if required (e.g. JACIE for cell & ex-vivo gene therapies, HTA for cell & tissue)
- Governance approvals in place

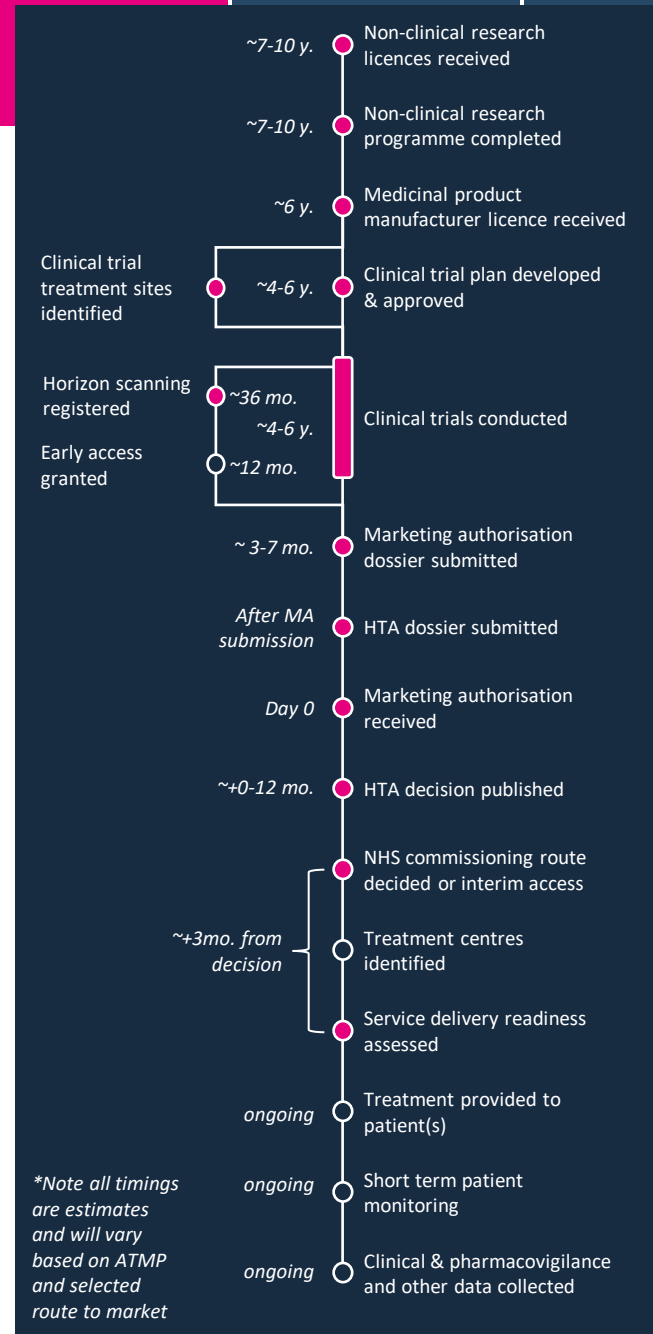
NSS will cascade treatment centre decision down to relevant NHS Scotland Health Boards and treatment centres. Once agreed, developers can engage with treatment centres to get service up and running (this process will vary depending on the type of ATMP)

Note: Not all ATMPs will require specialised services and may also be provided by health boards in line with routine use. Selection is based on specific needs of the medicine and existing capabilities of treatment centres.

For clinical trials, treatment centre identification is determined by the developer and may be driven by the expertise or reputation of a particular centre or physician working in the disease area.

*NSS may also decide to provide the treatment through Specialist Services UK, whereby Scottish Patients are funded for treatment in England through a service agreement

Linked steps | Who is involved? | Best practices & tips | Back to England



# 1 What can be done to prepare for ATMP service provision?

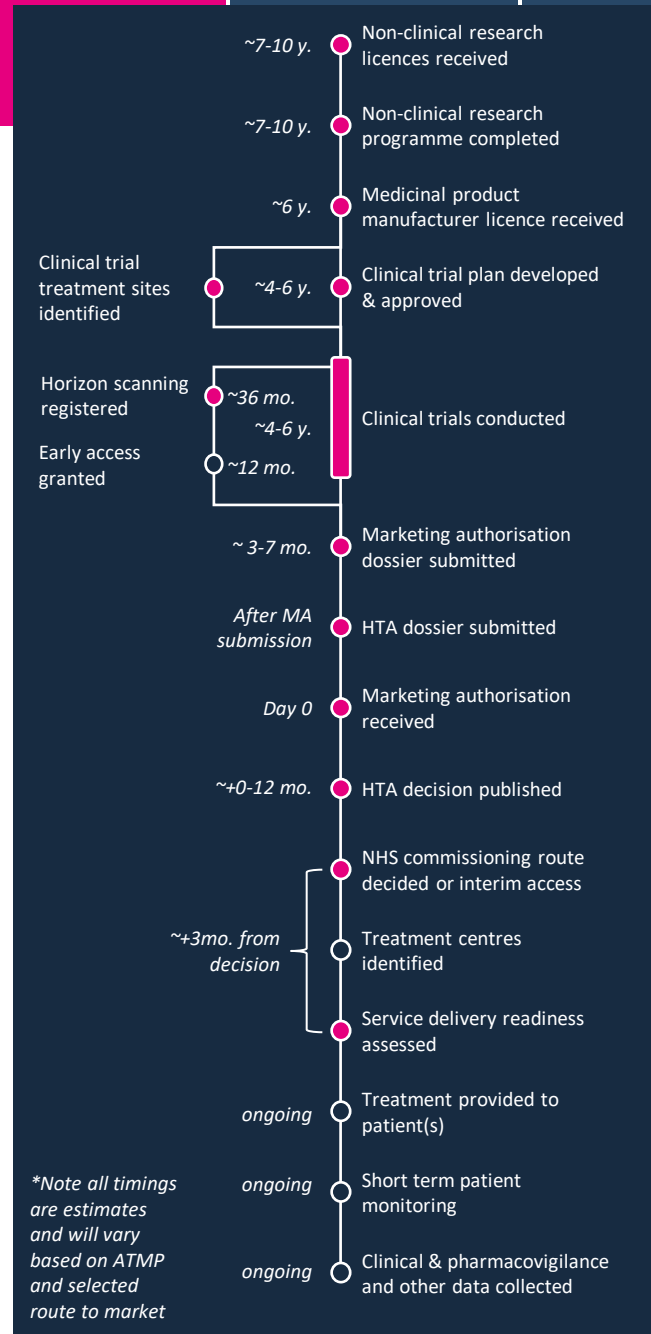
**KEY TOPICS**

**Treatment centre identification (Scotland)**

Overview | **To-do list** | Output

- Engage with NHS Scotland Health Boards and treatment centres once decision received from NSS

**When**
After positive recommendation received from SMC




Linked steps | Who is involved? | Best practices & tips | Back to England

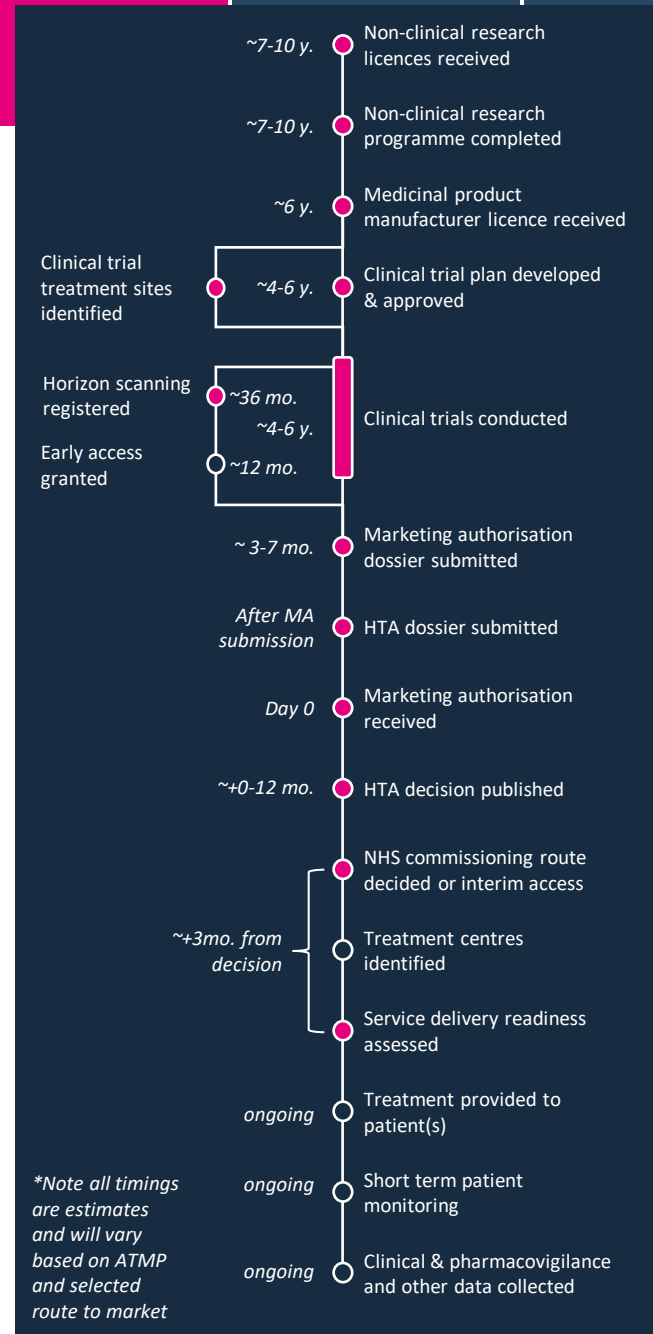
# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

**Treatment centre identification (Scotland)**

Overview | To-do list | **Output**

- Treatment centres identified for ATMP provision




Linked steps | Who is involved? | Best practices & tips | Back to England

# 1 What can be done to prepare for ATMP service provision?

## KEY TOPICS

**Treatment centre identification (Scotland)**

Overview

To-do list

Output

Routine commissioning

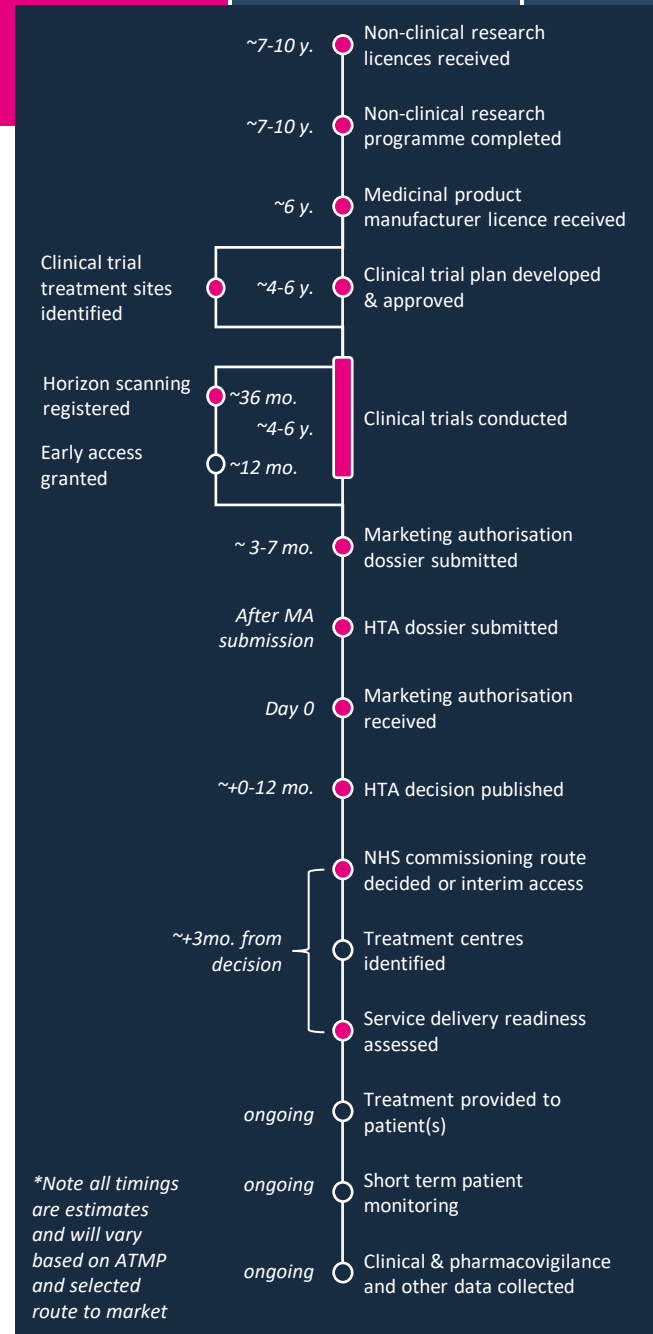
Commissioning via Managed Access

Linked steps

Who is involved?

Best practices & tips

Back to England



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

**Treatment centre identification (Scotland)**

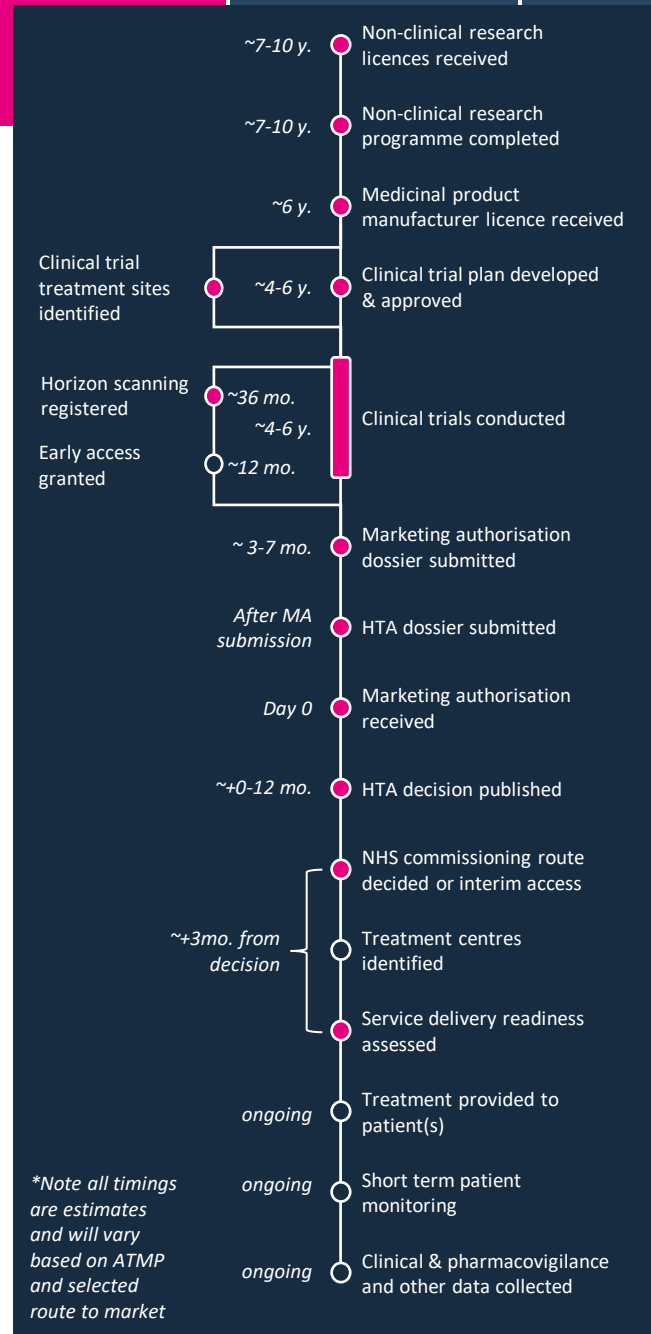
## Overview

- ATMP developer
- National Services Scotland
- Regional and local hospital management teams

## To-do list

## Output

**Linked steps** | **Who is involved?** | **Best practices & tips** | **Back to England**



# 1 What can be done to prepare for ATMP service provision?

**KEY TOPICS**

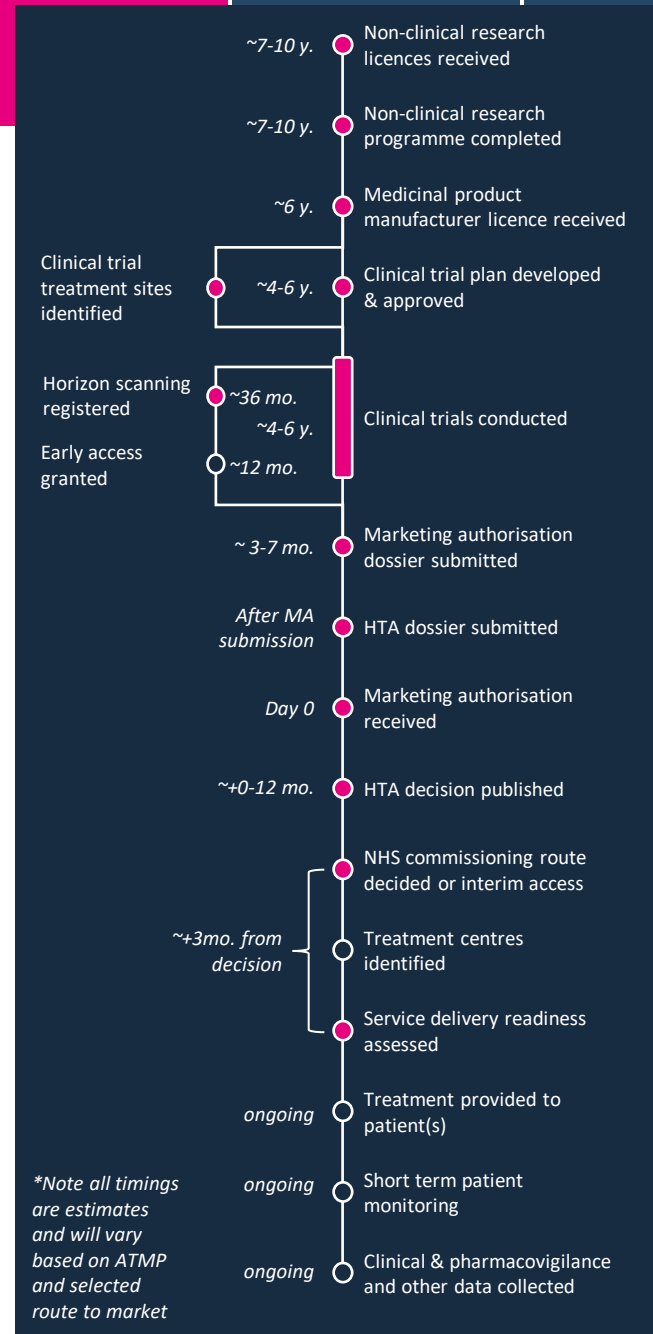
**Treatment centre identification (Scotland)**

Overview

To-do list

Output

**Linked steps** | **Who is involved?** | **Best practices & tips** | **Back to England**



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

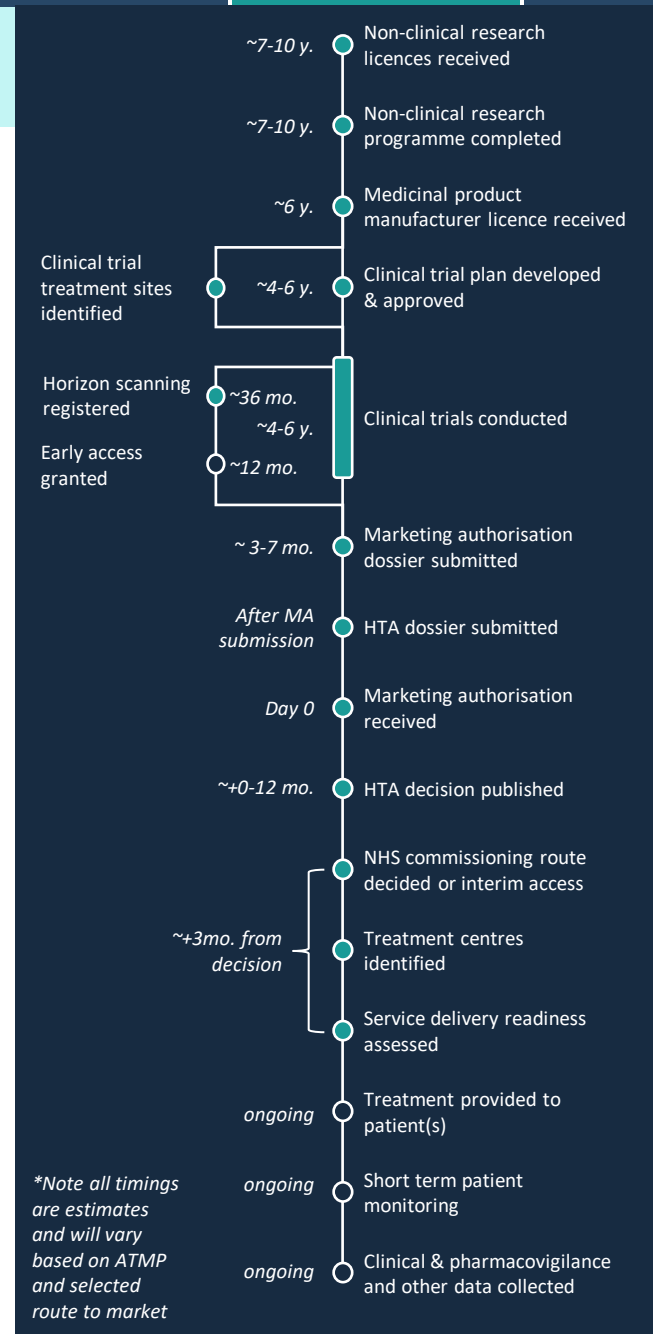
## KEY TOPICS

- **Treatment provision (Cell Therapies)**
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

**Overview** | To-do list | Output

Developers and NHS treatment centres should review Specialist Pharmacy Service (SPS) pharmacy institutional readiness guidance for Somatic Cell Therapies. The checklists involved may be used in preparation for, and during treatment provision, or as informative guidance as to how to customise in-centre processes to ensure that all relevant factors and requirements are considered.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- **Treatment provision (Cell Therapies)**
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

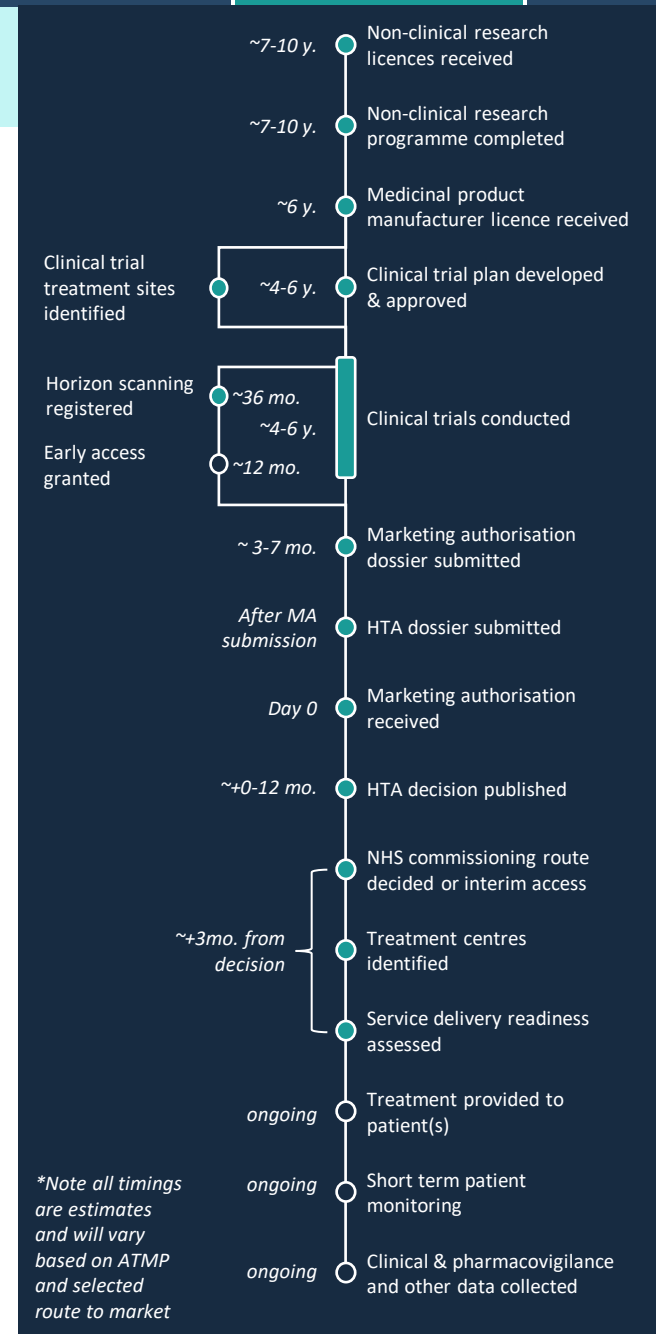
Overview | **To-do list** | Output

- Review SPS pharmacy institutional readiness guidance for Somatic Cell Therapies here
- These documents contain the following checklists which may be useful for treatment centres:
  - sCTMP Pharmacy Medicines Management Checklist
  - sCTMP in Pharmacy Patient Referral Checklist
  - sCTMP in Pharmacy Patient Approval Checklist
  - sCTMP Receipt Checklist
  - sCTMP Stem Cell Lab / Outsourced Aseptic Preparation Checklist
  - sCTMP Clinical Area Preparation Checklist
  - sCTMP Pharmacy Patient Dispensing Checklist
- Review SPS guidance for out-of-specification ATMPs here

**When**

Review guidance prior to NICE HTA assessment. Resources for use and implementation after positive recommendation received from NICE

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- **Treatment provision (Cell Therapies)**
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

Overview | To-do list | **Output**

- ATMP product availability within the NHS


Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype

**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

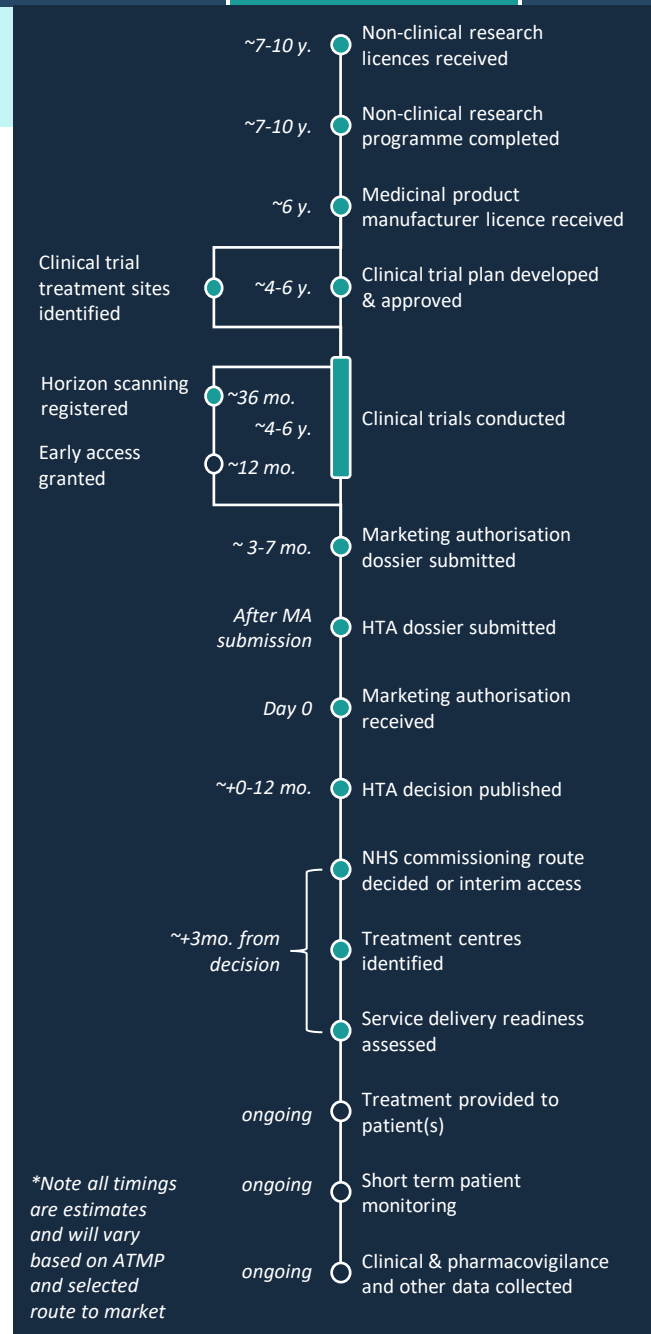
- **Treatment provision (Cell Therapies)**
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

Overview | To-do list | Output

Service delivery readiness

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

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## KEY TOPICS

- **Treatment provision (Cell Therapies)**
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

## Overview

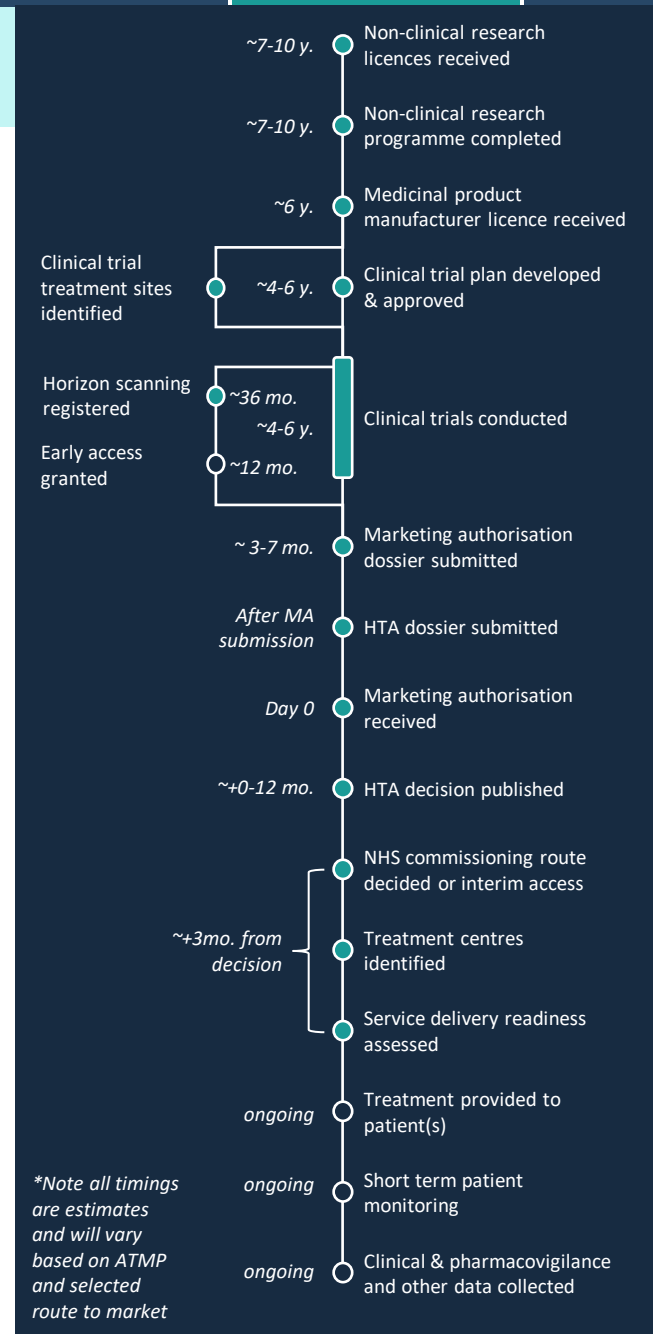
- NHS treatment centres
- ATMP developers
- NHSE

## To-do list

## Output

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

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## KEY TOPICS

- **Treatment provision (Cell Therapies)**
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- Short-term patient monitoring

Overview

To-do list

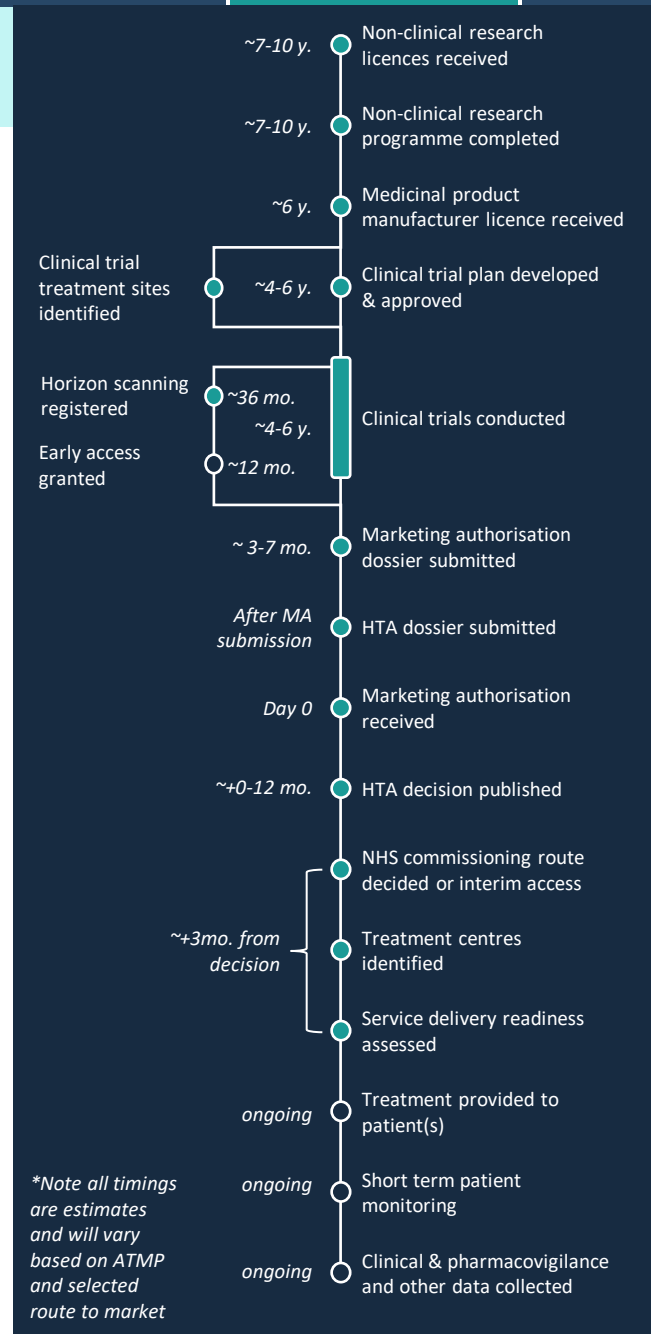
Output

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

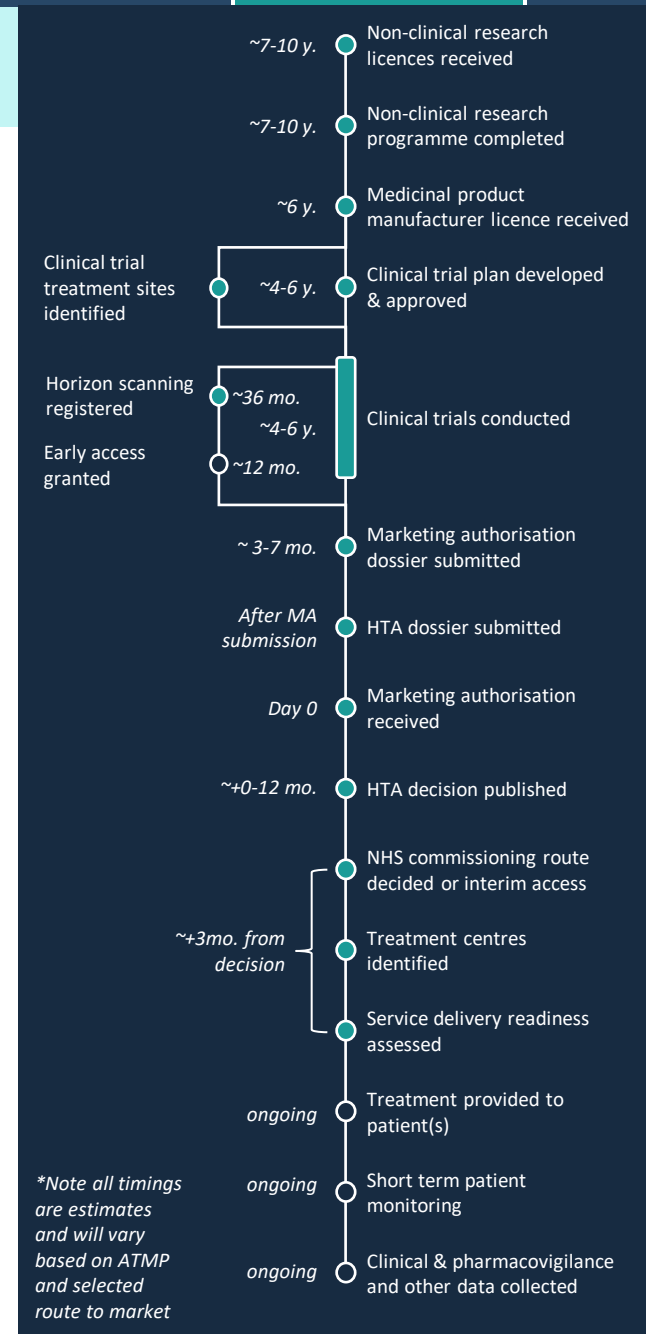
2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- **Treatment provision (Gene Therapies)**
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

**Overview** | To-do list | Output

Developers and NHS treatment centres should review Specialist Pharmacy Service (SPS) pharmacy institutional readiness guidance for *in vivo* or *ex vivo* gene therapies. The checklists involved may be used in preparation for, and during treatment provision, or as informative guidance as to how to customise in-centre processes to ensure that all relevant factors and requirements are considered.




Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype

**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

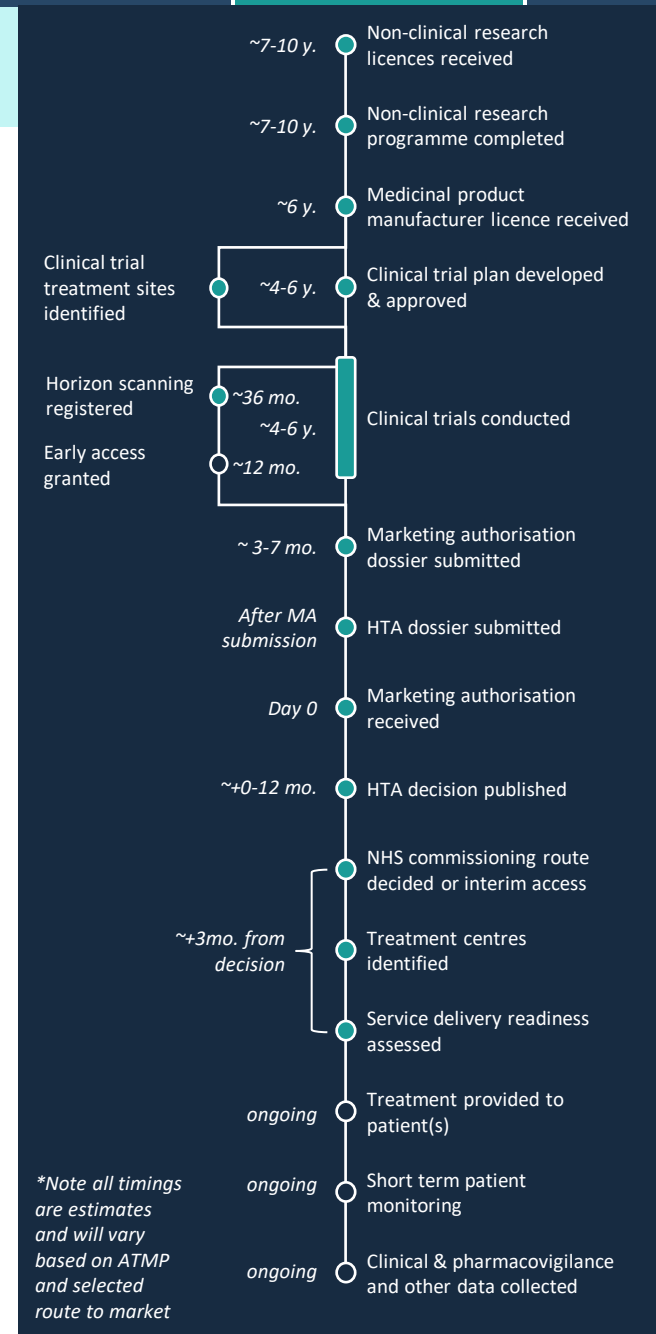
- Treatment provision (Cell Therapies)
- **Treatment provision (Gene Therapies)**
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

Overview | **To-do list** | Output

- Review SPS pharmacy institutional readiness guidance
  - For *ex vivo* (cell based) gene therapies here
  - For *in vivo* (virus based) gene therapies here
- These documents contain the following checklists which may be useful for treatment centres:
  - *Ex vivo* or *in vivo* GTMP Pharmacy Medicines Management
  - Checklist
  - *Ex vivo* or *in vivo* GTMP Pharmacy Class and Containment Checklist
  - *Ex vivo* or *in vivo* GTMP Pharmacy Patient Referral Checklist
  - *Ex vivo* or *in vivo* GTMP Pharmacy Patient Approval Checklist
  - *Ex vivo* or *in vivo* GTMP Receipt Checklist
  - *Ex vivo* Stem Cell Lab / Outsourced Aseptic Preparation Checklist or *in vivo* GTMP Pharmacy Aseptic Preparation Checklist
  - *Ex vivo* or *in vivo* Clinical Area Preparation Checklist
  - *Ex vivo* or *in vivo* Pharmacy Patient Dispensing Checklist
- Review SPS guidance for out-of-specification ATMPs here

**When**

Review guidance prior to NICE HTA assessment. Resources for use and implementation after positive recommendation received from NICE.




Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- **Treatment provision (Gene Therapies)**
- Treatment provision (Tissue Engineered Products)
- Short-term patient monitoring

Overview | To-do list | **Output**

- ATMP product availability within the NHS


Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype

**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
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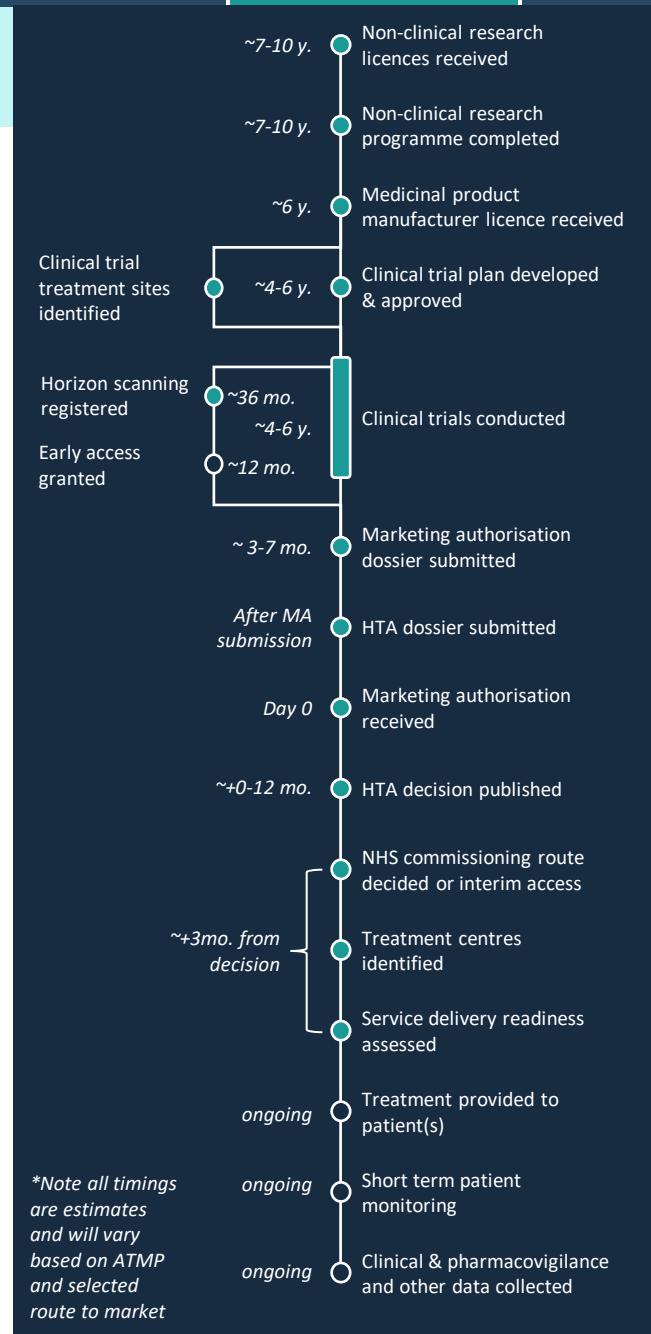
- Short-term patient monitoring

Overview | To-do list | Output

Service delivery readiness

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



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## KEY TOPICS

- Treatment provision (Cell Therapies)
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- Short-term patient monitoring

## Overview

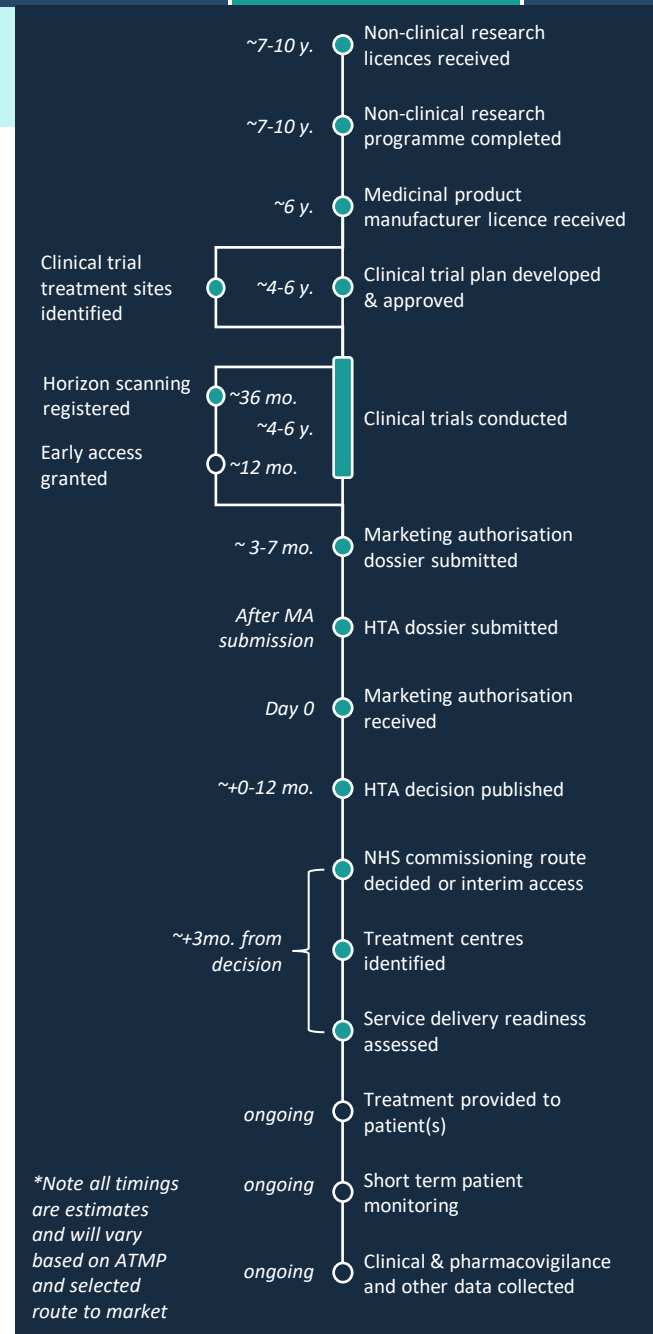
- NHS treatment centres
- ATMP developers
- NHSE

## To-do list

## Output

Linked steps | Who is involved? | Best practices & tips

**Variation by ATMP archetype**



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## KEY TOPICS

- Treatment provision (Cell Therapies)
- **Treatment provision (Gene Therapies)**
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- Short-term patient monitoring

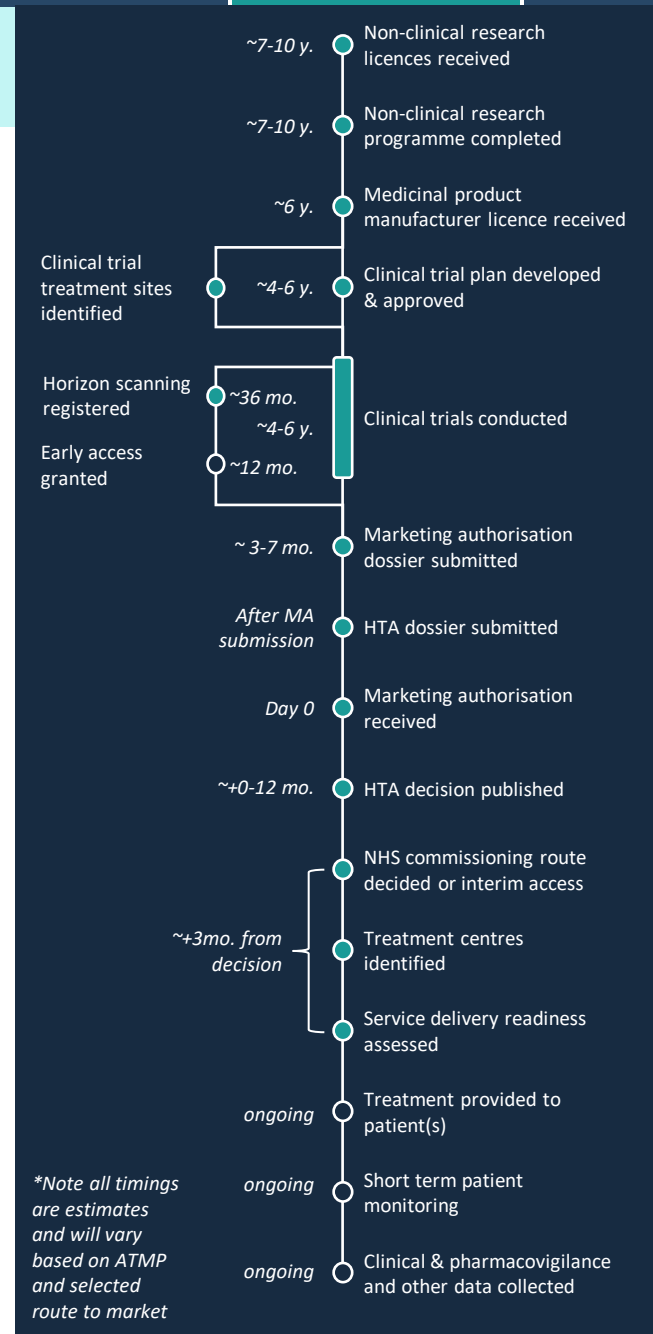
Overview

To-do list

Output

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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2 What follow-up activities are required after patient treatment?

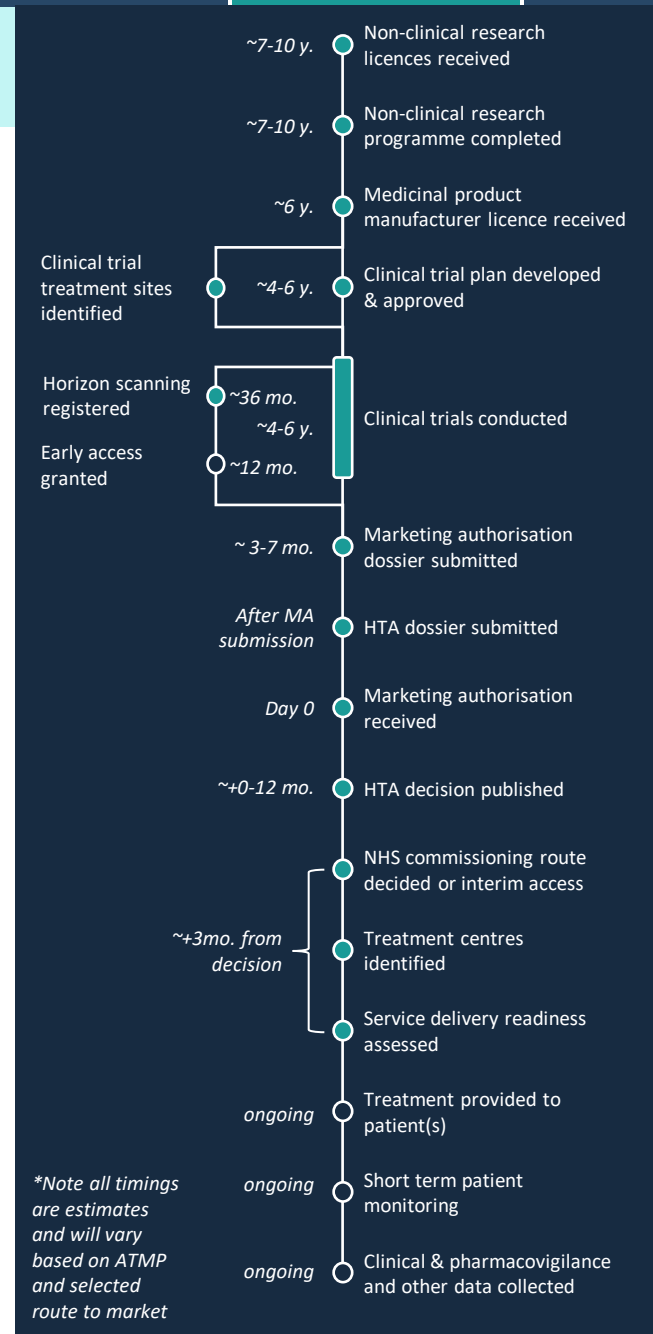
## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- **Treatment provision (Tissue Engineered Products)**
- Short-term patient monitoring

**Overview** | To-do list | Output

Developers and NHS treatment centres should review Specialist Pharmacy Service (SPS) pharmacy institutional readiness guidance for Tissue Engineered Products. The checklists involved may be used in preparation for, and during treatment provision, or as informative guidance as to how to customise in-centre processes to ensure that all relevant factors and requirements are considered.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS



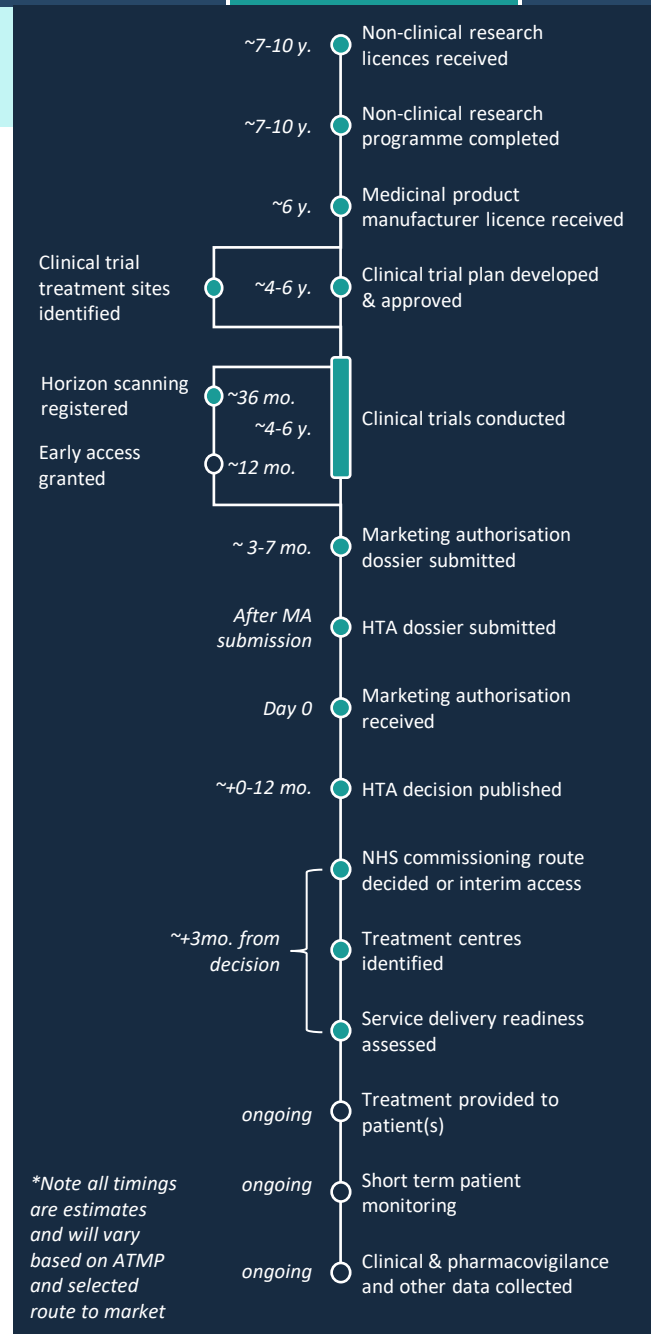
Overview | **To-do list** | Output

- Review SPS pharmacy institutional readiness guidance for Tissue Engineered Products here
- These documents contain the following checklists which may be useful for treatment centres:
  - TEP Pharmacy Medicines Management Checklist
  - TEP Pharmacy Patient Referral Checklist
  - TEP Pharmacy Patient Approval Checklist
  - TEP Receipt Checklist
  - TEP Pharmacy Patient Dispensing and Shipping Checklist
- Review SPS guidance for out-of-specification ATMPs here

**When**

Review guidance prior to NICE HTA assessment. Resources for use and implementation after positive recommendation received from NICE.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

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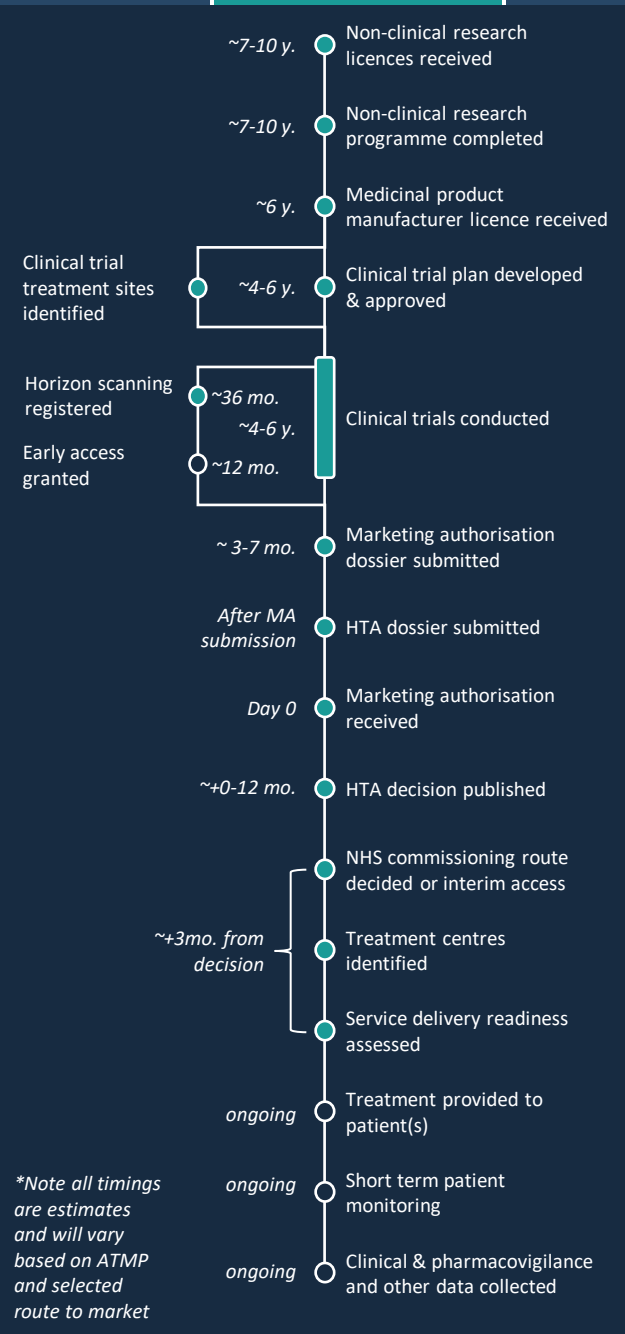
## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- **Treatment provision (Tissue Engineered Products)**
- Short-term patient monitoring

Overview | To-do list | **Output**

- ATMP product availability within the NHS



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## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- **Treatment provision (Tissue Engineered Products)**
- Short-term patient monitoring

## Overview

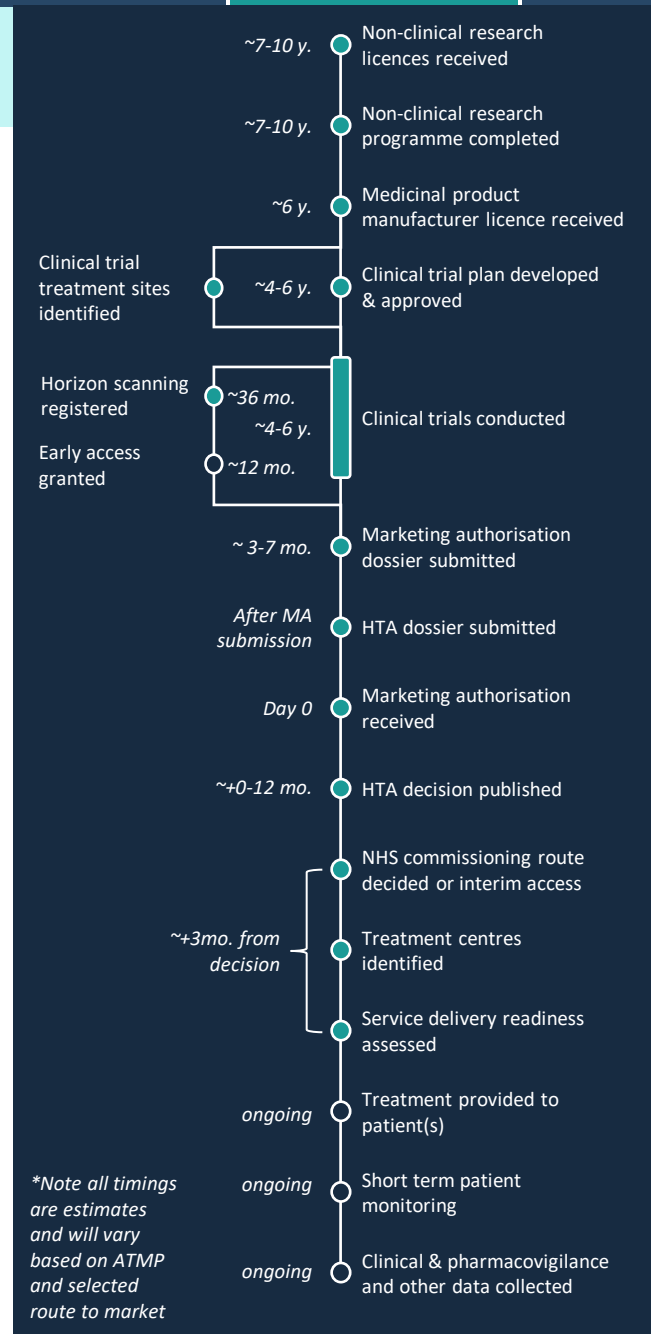
## To-do list

## Output

Service delivery readiness

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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## KEY TOPICS

- Treatment provision (Cell Therapies)
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- Short-term patient monitoring

## Overview

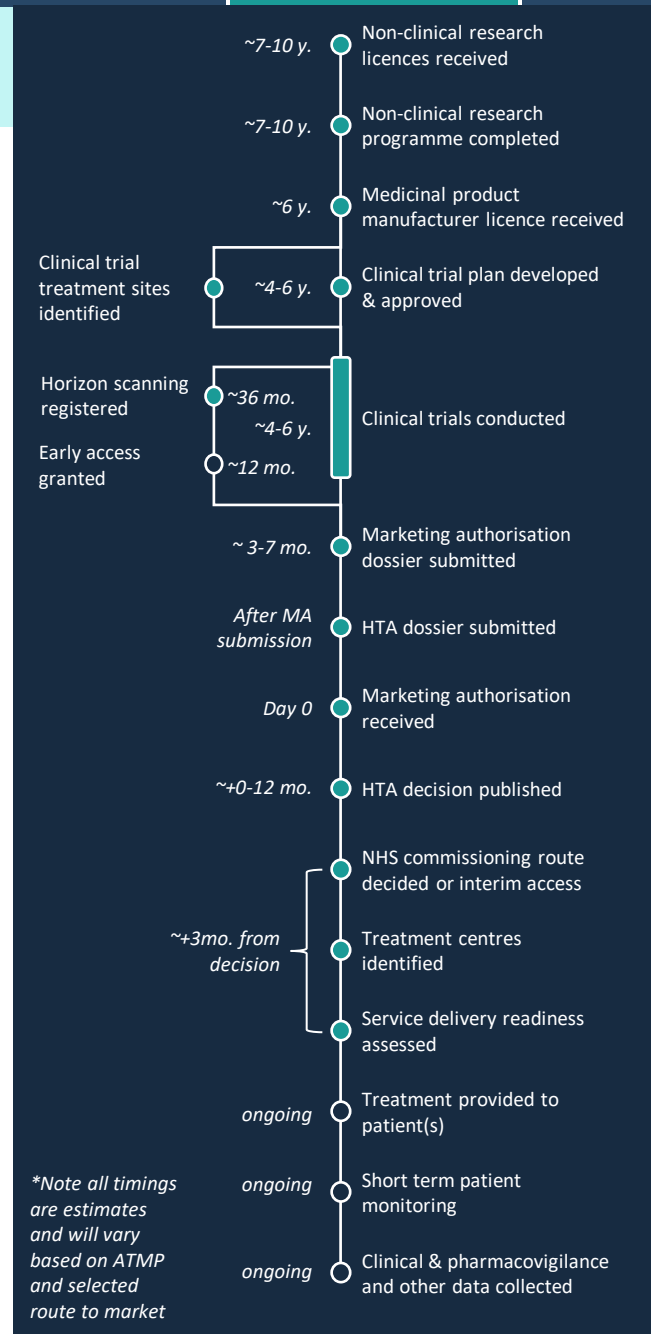
## To-do list

## Output

- NHS treatment centres
- ATMP developers
- NHSE

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



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## KEY TOPICS

- Treatment provision (Cell Therapies)
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- **Treatment provision (Tissue Engineered Products)**
- Short-term patient monitoring

Overview

To-do list

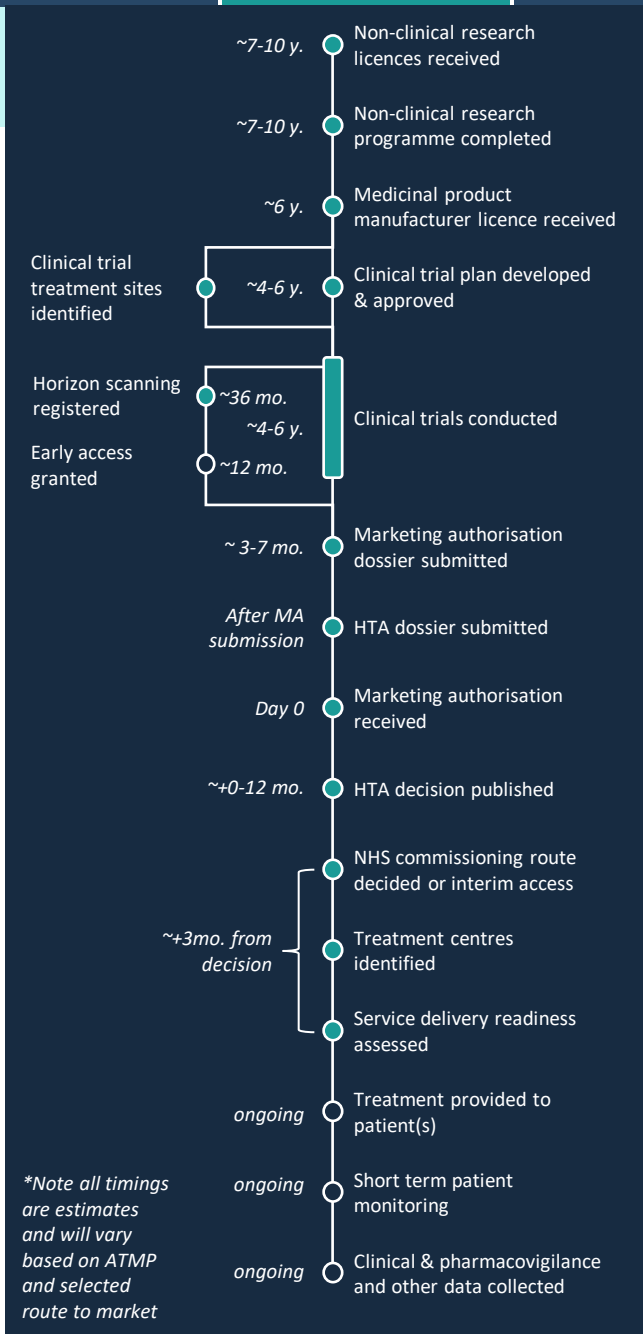
Output

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

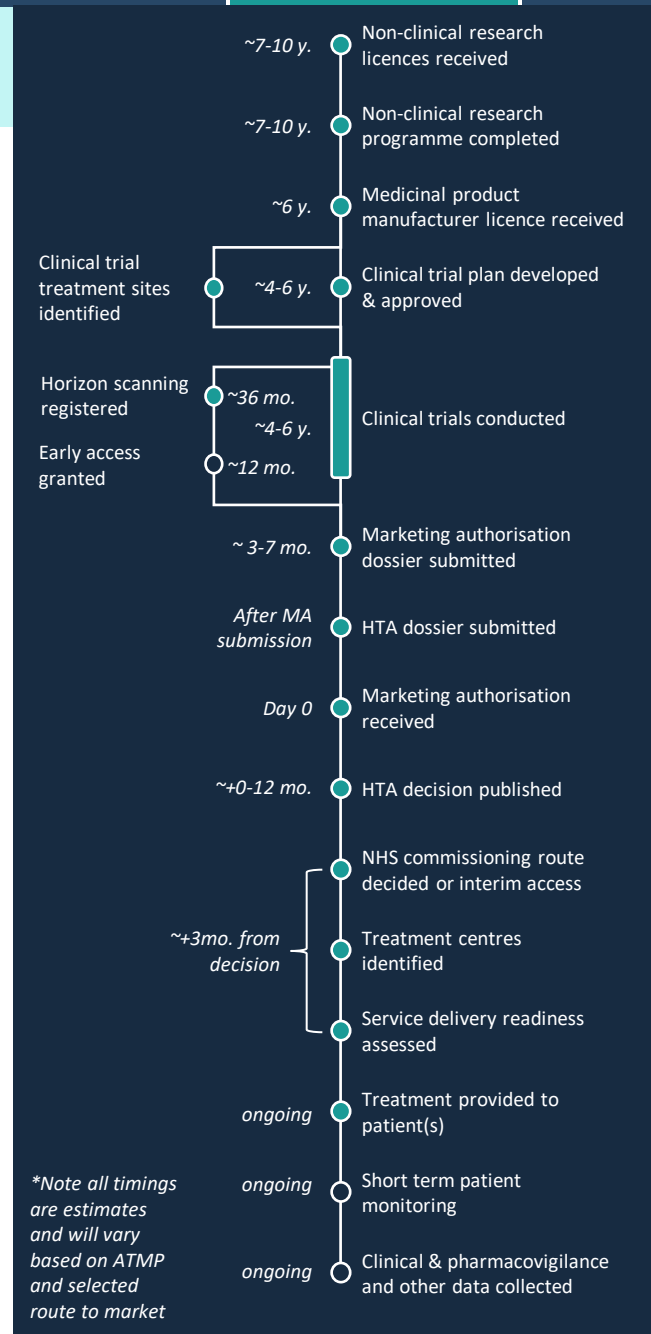
**Overview** | To-do list | Output

As part of patient treatment, NHS treatment centres and healthcare professionals will monitor patients for adverse events in both the short and long term.

NHS treatment centres will have their own processes and patient monitoring procedures, and these will have been considered as part of service delivery readiness.

The MHRA also operates the Yellow Card Scheme, which allows healthcare professionals and patients to report a side effect or adverse event from a medicine or medical device.

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

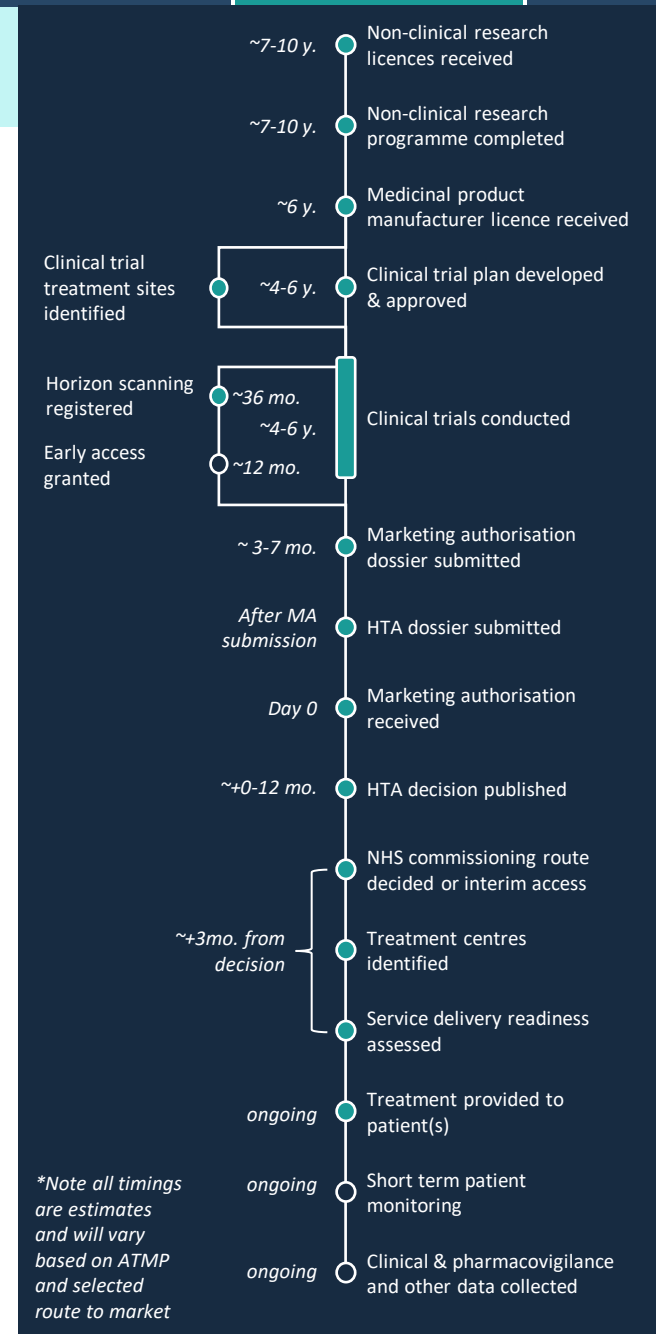
Overview | **To-do list** | Output

- Guidance on adverse event monitoring can be found here
- If applicable, report the advert event to the MHRA yellow card scheme here
- Guidance on reporting to the yellow card scheme can be found here
- In-hospital monitoring processes and procedures should be in line with Good Clinical Practice guidelines

**When**

After ATMP treatment administration

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

Overview | To-do list | **Output**

- Adverse events reported to the MHRA
- Adverse events recorded as part of hospital processes within patient medical record


Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype

**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

## Overview

GxP compliance & certification

Service delivery readiness

## To-do list

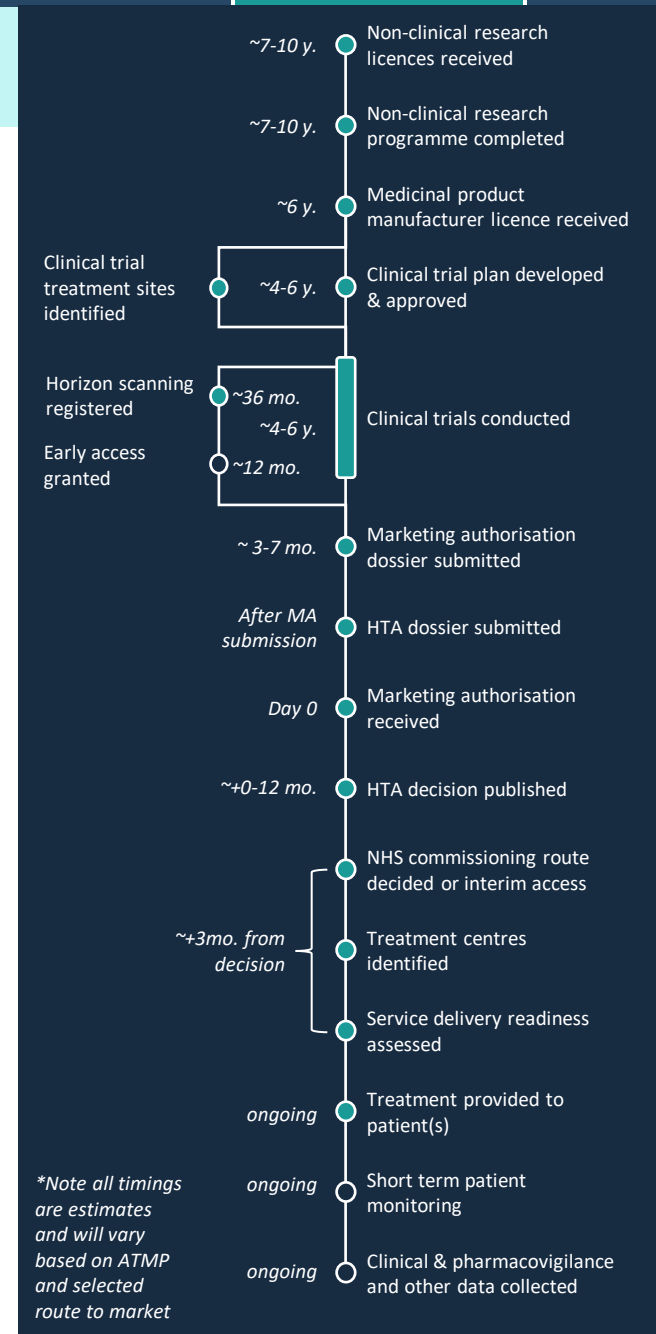
## Output

Linked steps

Who is involved?

Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

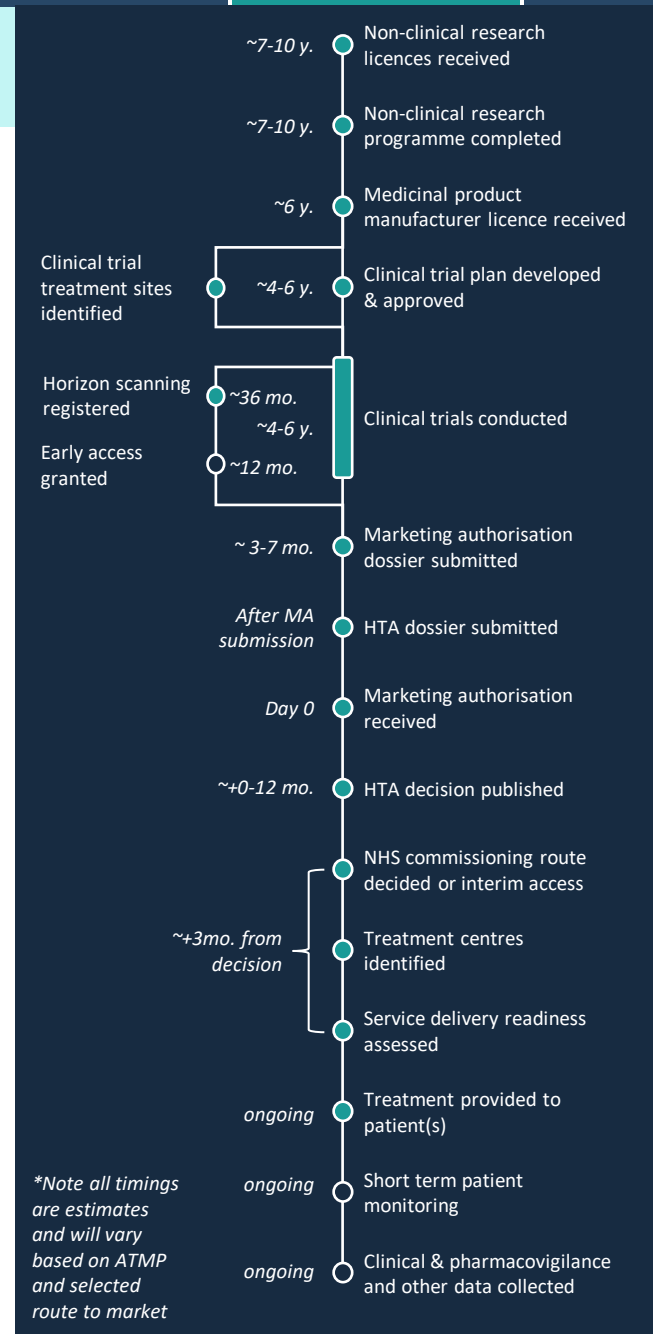
- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

Overview | To-do list | Output

- NHS healthcare professionals

Linked steps | Who is involved? | Best practices & tips

Variation by ATMP archetype



**1 What key steps are required to provide ATMPs to patients?**

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

- Treatment provision (Cell Therapies)
- Treatment provision (Gene Therapies)
- Treatment provision (Tissue Engineered Products)
- **Short-term patient monitoring**

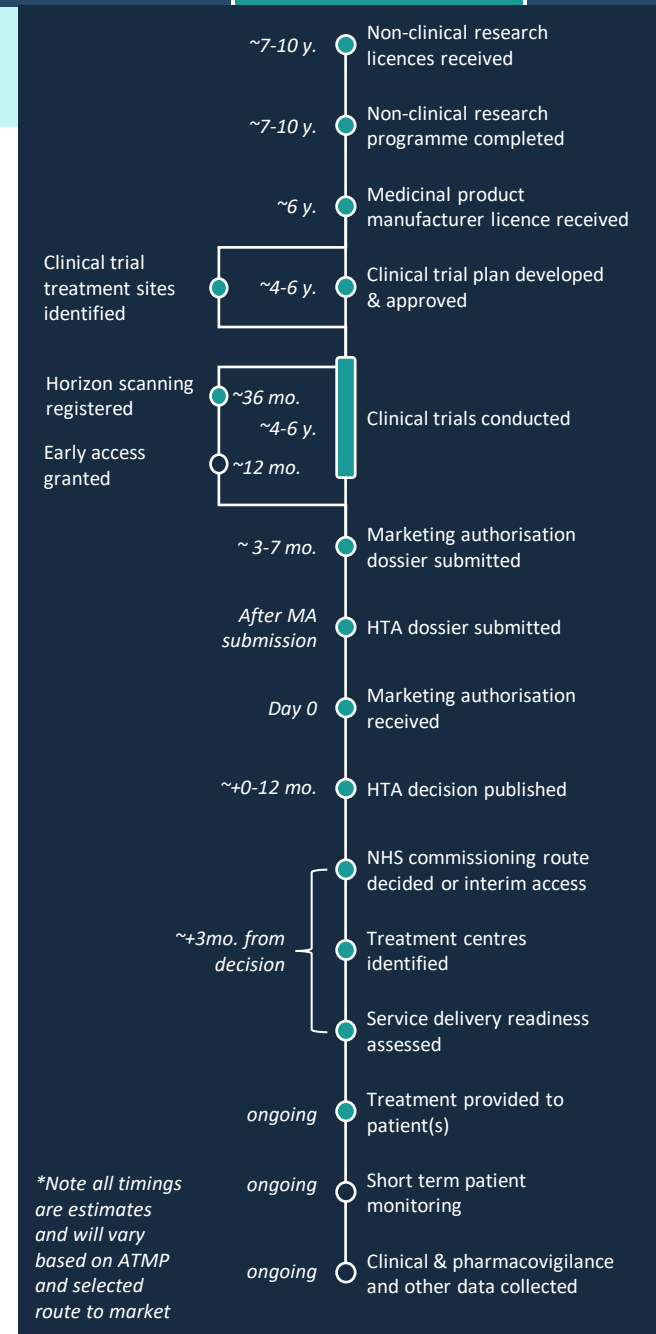
Overview

To-do list

Output

**Linked steps** | **Who is involved?** | **Best practices & tips**

**Variation by ATMP archetype**



1 What key steps are required to provide ATMPs to patients?

2 What follow-up activities are required after patient treatment?

## KEY TOPICS

**Data collection**

**Overview** | To-do list | Output

Developers, NHS treatment centre providers, and other ecosystem partners (e.g. NICE, MHRA, if applicable) should ensure that there is alignment on which stakeholders are responsible for data collection and over what time period.

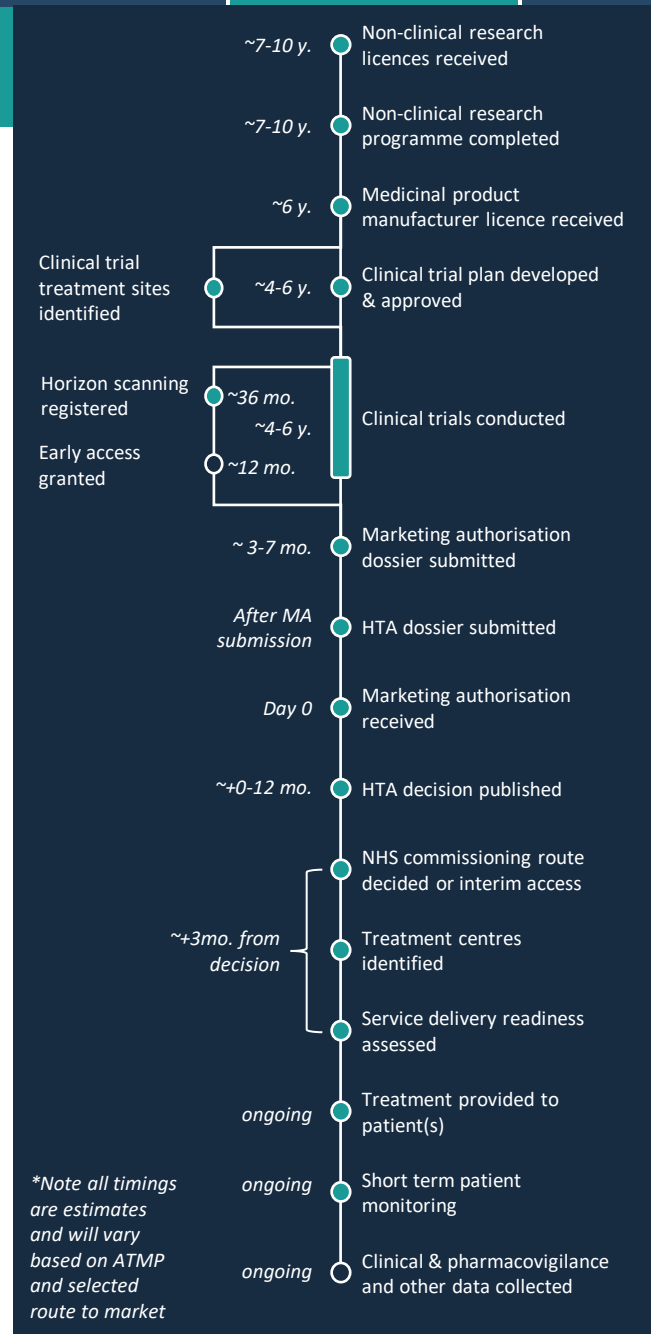
NHS treatment centres and the developer will then be responsible for ongoing safety, clinical efficacy and other data collection (e.g. PROMs/PREMs), which may also involve reporting to disease-specific or product-specific patient data registries and data collection agencies.

Ongoing patient data collection may be required as part of:

- Continued treatment centre accreditation (e.g. JACIE/EBMT)
- Regulatory requirements or conditions included as part of Marketing Authorisation
- Mandated data collection for products which have Managed Access Agreements as set out in the Data Collection Arrangement
- Treatment centre-level agreements with developers if data collection is required and/or if value-based contracts are in place

Data collection should continue until such time as it is no longer mandated by any of the above (or in case of a Managed Access Arrangement at the point agreed in the Data Collection Arrangement)

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



1 What key steps are required to provide ATMPs to patients?

2 What follow-up activities are required after patient treatment?

**KEY TOPICS**

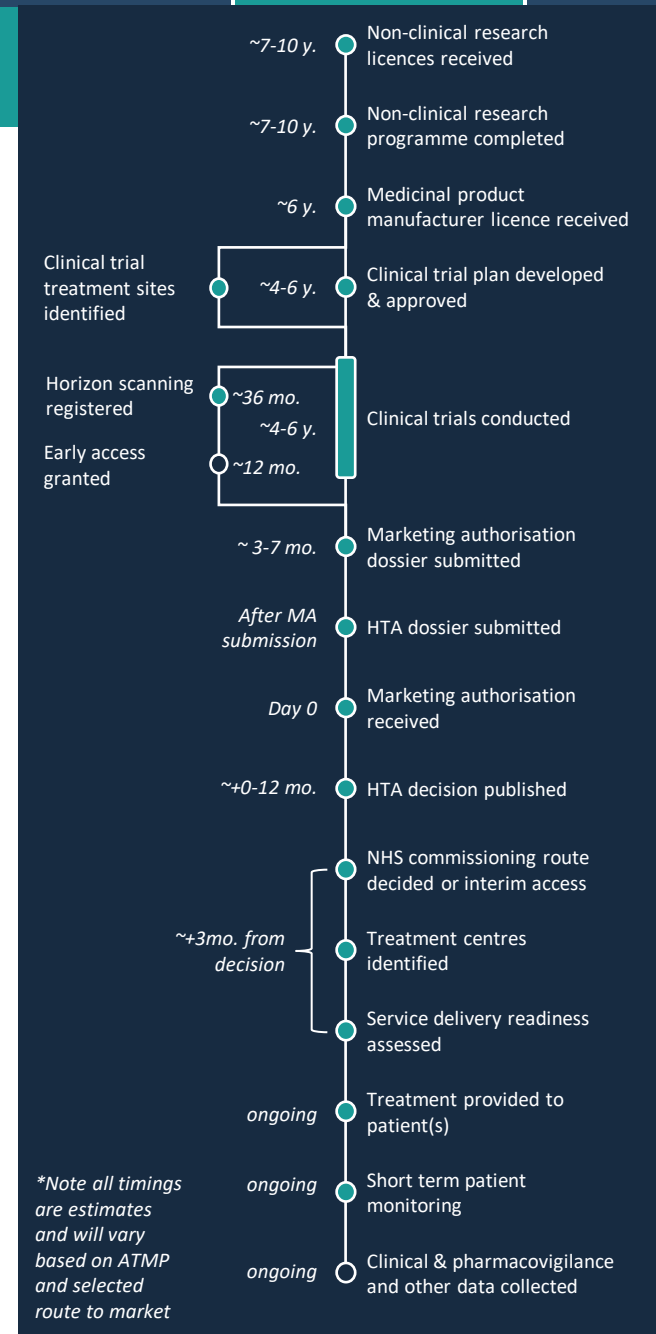
**Data collection**

Overview | **To-do list** | Output

- Ensure that treatment follow-up data is being collected as part of statutory, regulatory or commercial requirements
- Review the EMA guidelines on safety and efficacy follow-up and risk management of ATMPs here

**When**

After ATMP treatment administration and until data collection is no longer required (whether by regulators, contracts, MAA, statutory duties, or any other requirement)



**1** What key steps are required to provide ATMPs to patients?

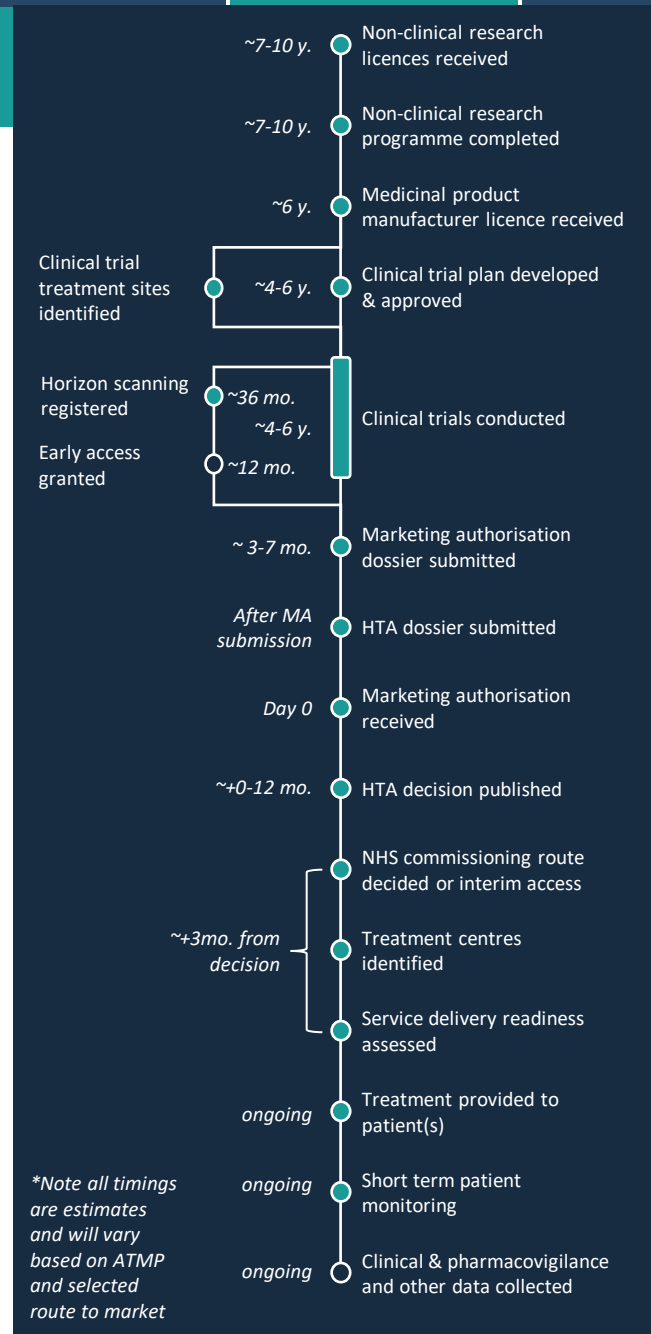
**2** What follow-up activities are required after patient treatment?

## KEY TOPICS

**Data collection**

Overview | To-do list | **Output**

- Ongoing patient data collection



**1** What key steps are required to provide ATMPs to patients?

**2** What follow-up activities are required after patient treatment?

## KEY TOPICS

**Data collection**

Overview

To-do list

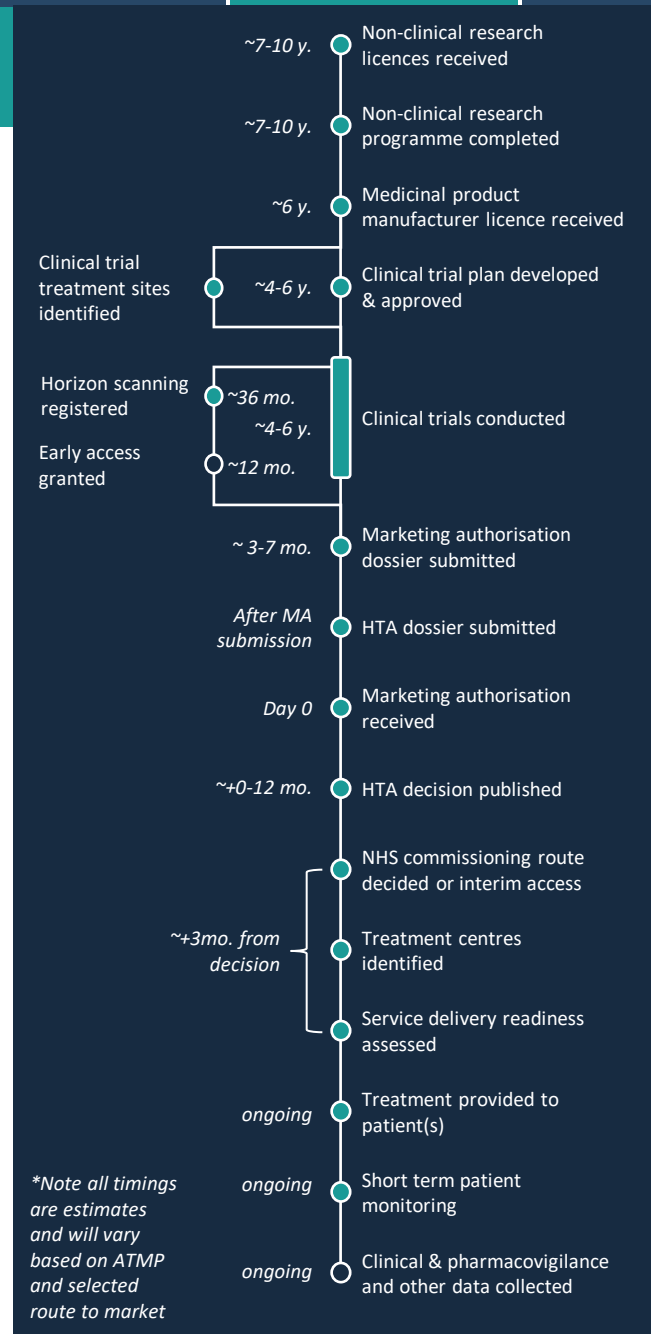
Output

Short term patient monitoring

Service delivery readiness

**Linked steps** **Who is involved?** **Best practices & tips**

**Variation by ATMP archetype**



**1** What key steps are required to provide ATMPs to patients?

**2** What follow-up activities are required after patient treatment?

**KEY TOPICS**

**Data collection**

Overview

- ATMP developer
- NHS treatment centres
- Data controller e.g. registries

To-do list

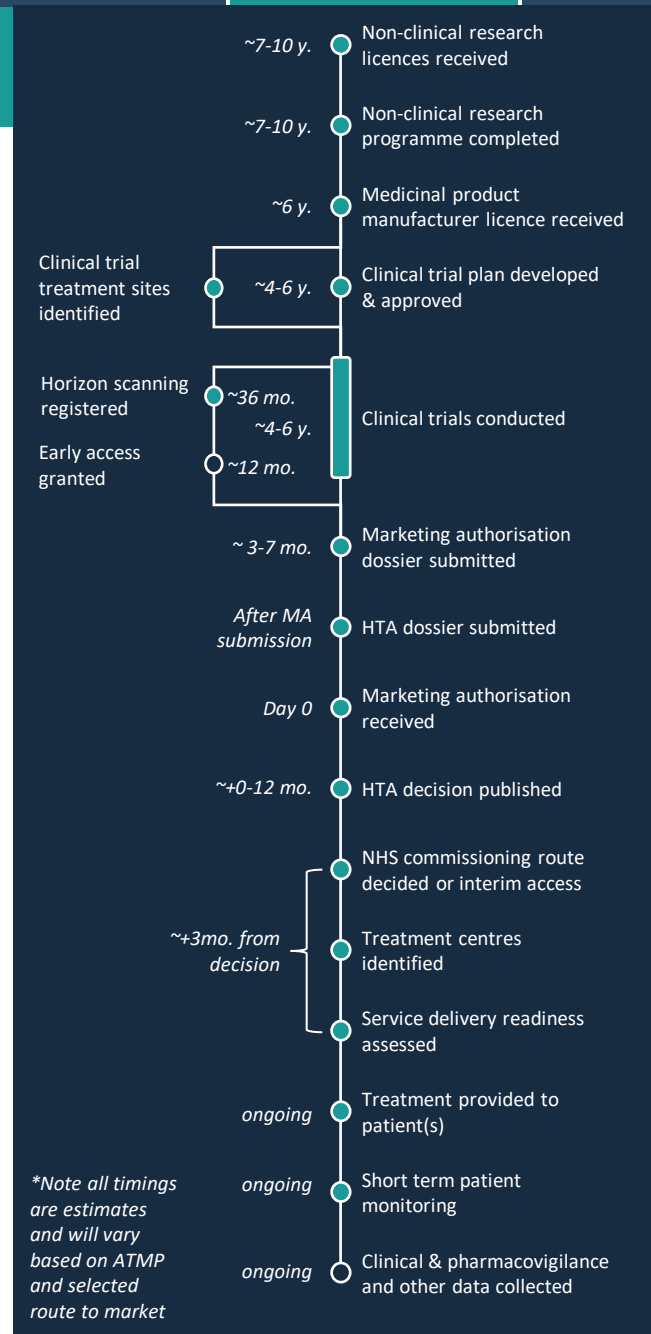
Output

**Linked steps**

**Who is involved?**

**Best practices & tips**

**Variation by ATMP archetype**



1 What key steps are required to provide ATMPs to patients?

2 What follow-up activities are required after patient treatment?

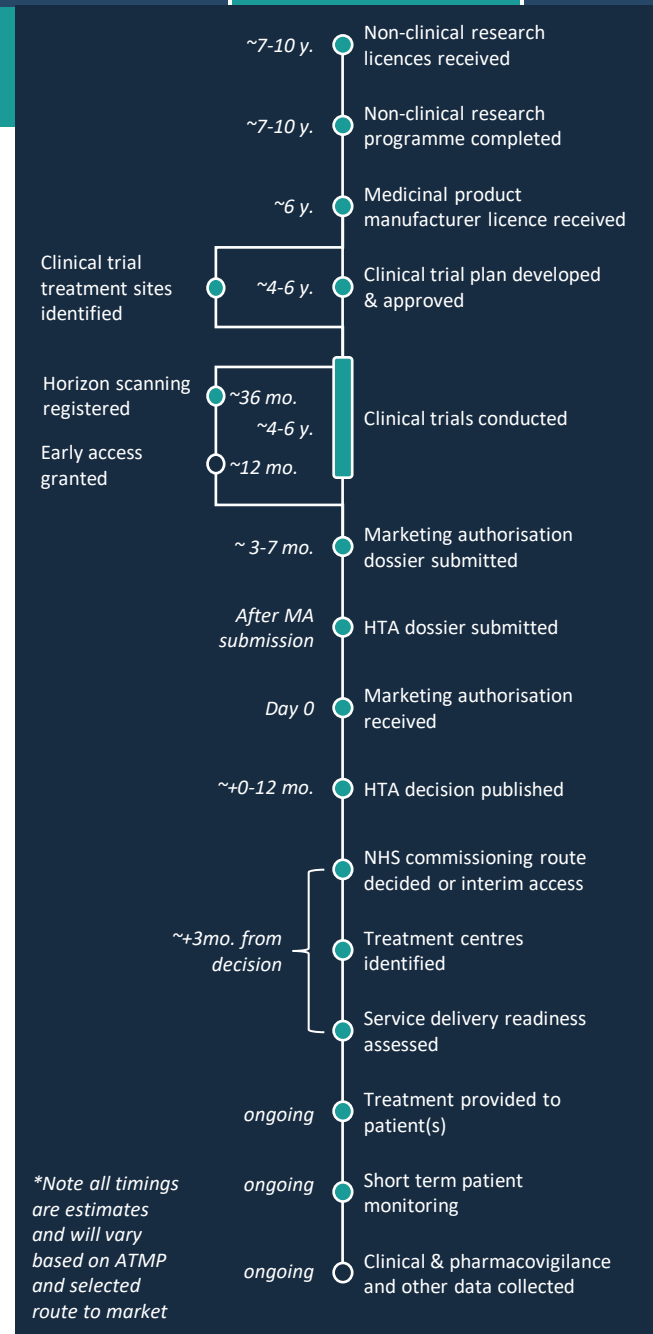
**KEY TOPICS**

**Data collection**

Overview | To-do list | Output

- Developers should ensure to consider long-term follow up of patients, and explore the availability of suitable digital infrastructure
- It is recommended to engage with patient groups to understand the impact on patients of long-term data collection and follow-up obligations
- See a report by Cancer Research UK on making outcomes-based payment a reality in the NHS here

Linked steps | Who is involved? | Best practices & tips | Variation by ATMP archetype



## Public and Patient Involvement & engaging with patient groups

Patient and public involvement should be included throughout the end-to-end ATMP pathway and should start as early as possible; engagement with patient groups will be key to product development. It is recommended that ATMP developers research and understand who are the key active organisations in their field or disease area. Below is a summary of the touchpoints with patient groups detailed throughout the pathway.

| | |
|---|---|
| *In vitro and in vivo* studies | Developers are advised to consider how to involve patient groups in the development phase to ensure that the ATMP product targets and addresses the priorities of those it intends to treat. |
| Delivery and diagnostic route assessment | Developers are advised to consult patient groups and use patient and public involvement (PPI) organisations to help refine the patient journey and diagnostic pathways. Links to useful guidance from National Institute for Health Research (NIHR) can be found here. |
| Clinical trial planning, design & protocol development | Consultation with patient groups through PPI is becoming increasingly important and may be considered as a key element in every developer's clinical trial design. Developers should also consider when to alert disease specific non-profit organisations supporting patients to notify them of upcoming treatments. |
| Informed consent procedure approval | When developing informed consent procedures, developers are advised to involve relevant patient groups for co-development. Documentation of this must be included in the dossier for ethics approval as part of the clinical trial application |
| Health Technology Assessment Technology Appraisal<br>Health Technology Assessment Highly Specialised Technologies evaluation | Patient groups and PPI will form an essential part of the scope preparation stage during HTA and input from patients and the community will be important in the appraisal process. |
| Data collection | It is recommended to engage with patient groups to understand the impact on patients of long-term data collection and follow-up obligations |

See this call to action for why it is important to include patient groups.
Other useful resources for PPI include:

- Findacure
- HTAI resources
- ABPI resources
- NIHR resources

Note: whilst it is critical to engage with patient groups and patient organisations, developers should remain conscious that the vast majority are volunteer-led and operated and may have limited resources. Developers are therefore advised to ensure that when engaging with patient organisations that they are fully prepared.

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| Stakeholder | What are they responsible for? |
|---|---|
| AAC | The NHS Accelerated Access Collaborative is a partnership between patient groups, government bodies, industry and NHS bodies, working together to streamline the adoption of new innovations in healthcare. AAC brings together industry, government, regulators, patients and the NHS to remove barriers and accelerate the introduction of ground-breaking new treatments. The AAC supports all types of innovations: medicines, diagnostics, devices, digital products, pathway changes and new workforce models. |
| ADTCC (Scotland) | All NHS boards in Scotland have an Area Drug and Therapeutics Committee (ADTC). ADTCs provide professional and clinical advice and leadership to NHS boards to support safe, clinically effective, cost effective and patient-centred use of medicines in all care settings. The ADTC Collaborative (ADTCC), hosted by Healthcare Improvement Scotland, was created to Strengthen clinical engagement, shared learning and collaboration between ADTCs. |
| AWMSG | The All Wales Medicines Strategy Group (AWMSG) advises Welsh Government about the use, management and prescribing of medicines in Wales. |
| CDF | The Cancer Drugs Fund (CDF) is a source of interim funding for cancer drugs in England. The CDF Provides patients with faster access to the most promising new cancer treatment and helps to ensure more value for money for taxpayers. |
| Cell and Gene Therapy Catapult | The Cell and Gene Therapy Catapult was established as an independent centre of excellence to advance the growth of the UK cell and gene therapy industry, by bridging the gap between scientific research and full-scale commercialisation. It offers leading-edge capability, technology and innovation to enable companies to take products into clinical trials and provide clinical, process development, manufacturing, regulatory, health economics and market access expertise. Its aim is to make the UK the most compelling and logical choice for UK and international partners to develop and commercialise these advanced therapies. |
| EMA | The European Medicines Agency (EMA) is a decentralised agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU. |

| Stakeholder | What are they responsible for? |
|---|---|
| FDA | The US Food and Drug Administration is a federal agency of the Department of Health and Human Services. The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices. |
| HRA | The Health Research Authority is an executive non-departmental public body of the Department of Health and Social care in the United Kingdom. The HRA exists to provide a unified national system for the governance of health research. They work together with organisations such as the MHRA in the UK to regulate different aspects of health and social care research. |
| HSE | The Health and Safety Executive is a UK government agency responsible for the encouragement, regulation and enforcement of workplace health, safety and welfare. |
| HTA | The Human Tissue Authority is a non-departmental public body of the Department of Health and Social Care, responsible for the regulation of organisations that remove, store and use human tissue for research, medical treatment, post-mortem examination, education and training, and display in public. The HTA is also responsible for providing approval for organ and bone marrow donations from living people. |
| JACIE | JACIE develops and maintain global standards for the provision of quality medical and laboratory practice in cellular therapy. Based on these standards, JACIE offers accreditation to transplant programmes in order to encourage health institutions and facilities to establish and maintain quality management systems impacting on all aspects of their activities and to engage in continuous improvement. |
| MHRA | The Medicines and Healthcare products Regulatory Agency (MHRA) regulates medicines, medical devices and blood components for transfusion in the UK. The Medicines and Healthcare products Regulatory Agency is an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe. |
| NHSE | NHS England commissions specialised services and oversees the budget, planning, delivery and day-to-day operation of the commissioning side of the National Health Service in England. |

| Stakeholder | What are they responsible for? |
|---|---|
| NICE | The National Institute for Health and Care Excellence (NICE) is an executive non-departmental public body of the Department of Health and Social Care in England, which produces evidence based guidance on the clinical and cost effectiveness of health technologies in England and Wales. |
| NIHR | The National Institute for Health Research is a United Kingdom government agency which funds research into health and care. |
| NSS | NHS National Services Scotland (NSS) is a Non Departmental Public Body which provides advice and services to the rest of NHS Scotland. Accountable to the Scottish Government, NSS works at the heart of the health service, providing national strategic support services and expert advice to NHS Scotland. |
| OMA | The Office for Market Access (OMA) is a service offered by NICE to provide the opportunity for life sciences companies to engage with NICE at an early stage in the product development and commercialisation process. |
| OWMAG | The One Wales Medicines Advisory Group (OWMAG) assesses the evidence collected by AWTTC and recommends the use of the medicine to the health board chief executives. If they endorse the recommendation, the decision applies across NHS Wales. |
| PASAG | The Patient Access Scheme Assessment Group (PASAG) reviews and advises NHS Scotland on the feasibility of proposed schemes for implementation. It operates separately from SMC to maintain the integrity of the assessment process. |
| PASLU | The Patient Access Schemes Liaison Unit (PASLU – part of the NICE Commercial Liaison Team) works with companies who are considering a patient access scheme for their drug or treatment. PASLU coordinate the review and evaluation of patient access scheme proposals and issue advice to NHS England and NHS Improvement (NHSE&I). |
| Patient groups | Patient groups are typically organised groups of patients and carers who meet to discuss practice issues and patient experience to improve the service. To provide a means for patients to become more involved and make suggestions about the healthcare services and products that they receive. Patient groups play a critical role in the drug development process and should be involved throughout the ATMP pathway. See more about their detailed involvement across the Roadmap here |

| Stakeholder | What are they responsible for? |
|---|---|
| SMC | The Scottish Medicines Consortium (SMC) provides advice to NHS Scotland about the value for patients of newly licensed medicines. SMC is part of Healthcare Improvement Scotland, the national healthcare improvement organisation for Scotland. SMC review new medicines that have received a licence from the MHRA, in addition to reviewing new formulations of, and new ways to use, established medicines. Before a medicine can be prescribed routinely in Scotland, it has to be accepted for use by SMC. |
| SPS | The NHS Specialist Pharmacy Service supports medicines optimisation across the NHS, with a key focus on high-cost, complex and innovative medicines and medicines-related services. The Pan UK Pharmacy Working Group for ATMPs is part of SPS, |
| UK Pharmascan | UK PharmaScan is a database of information on new medicines, indications, and formulations in the pharmaceutical pipeline. It is the primary source of information used by all of the UK's national horizon scanning organisations and NHS England to enable early engagement in planning and preparing the NHS for the introduction of new medicines, and to support faster NHS adoption. |
| WHSSC | The Welsh Health Specialised Services Committee (WHSSC) is a joint committee of each Local Health Board (LHB) in Wales. The Joint Committee brings Local Health Boards in Wales together to plan specialised services for the population of Wales. |



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| Acronym | Name |
|---|---|
| AAC | Accelerated Access Collaborative |
| ABPI | Association of the British Pharmaceutical Industry |
| ADTCC | Area Drug and Therapeutics Committee Collaborative |
| ANVISA | Agência Nacional de Vigilância Sanitária |
| ATMP | Advanced Therapy Medicinal Product |
| ATTC | Advanced Therapy Treatment Centre Network |
| AWMSG | All Wales Medicines Strategy Group |
| AWTTC | All Wales Therapeutics and Toxicology Centre |
| CAA | Commercial Access Agreement |
| CAT | Committee for Advanced Therapies |
| CDF | Cancer Drugs Fund |
| CE | Conformité Européenne (European Conformity) |
| CHM | Commission on Human Medicines |
| CHMP | Committee for Medicinal Products for Human Use |
| CRO | Contract Research Organisation |
| CTA | Clinical Trial Application |
| CTBVEAG | Clinical Trials, Biologicals & Vaccines Expert Advisory Group |
| CTIMP | Clinical Trial of an Investigational Medicinal Product |
| DAD | Decision Advice Document, Scottish FAD |
| DHSC | Department of Health and Social Care |
| DSUR | Development Safety Update Report |

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| Acronym | Name |
|---|---|
| EAG | Expert Advisory Group |
| EAMS | Early Access to Medicines Scheme |
| EBMT | European Society for Blood and Marrow Transplantation |
| eCTD | electronic Common Technical Document |
| EMA | European Medicines Agency |
| ERG | Evidence Review Group |
| FAD | Final Appraisal Document |
| FDA | Food and Drug Administration |
| FED | Final evaluation determination |
| FIH | First in Human |
| GCP | Good Clinical Practice |
| GLP | Good Laboratory Practices |
| GLPMA | Good Laboratory Practice Monitoring Authority |
| GMO | Genetically Modified Organism |
| GMP | Good Manufacturing Practices |
| GMS | Genomic Medicine Service |
| GTAC | Gene Therapy Advisory Committee |
| GTMP | Gene Therapy Medicinal Product |
| GPVP | Good Pharmacovigilance Practice |
| GxP | Good [insert field] Practice |
| HRA | Health Research Authority |

| Acronym | Name |
|---|---|
| HSCB | Health and Social Care Board |
| HSE | Health and Safety Executive |
| HST | Highly Specialised Technology |
| HTA | Human Tissue Authority |
| HTA | Health Technology Assessment |
| ICSR | Individual Case Safety Reports |
| ILAP | Innovative Licensing and Access Pathway |
| IMF | Innovative Medicines Fund |
| IMP | Investigational Medicinal Product |
| IRAS | Integrated Research Application System |
| ISRCTN | International Standard Randomised Controlled Trial Number |
| JACIE | Joint Accreditation Committee ISCT-Europe |
| MA | Marketing Authorisation |
| MAA | Managed Access Agreement |
| MHRA | Medicines and Healthcare products Regulatory Agency |
| NAS | New Active Substance |
| NDC | New Drugs Committee of the SMC |
| NHSE | National Health Service England |
| NHSE&I | National Health Service England & National Health Service Improvement |
| NIBSC | National Institute for Biological Standards and Control |
| NICE | National Institute for Health and Care Excellence |



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| Acronym | Name |
|---|---|
| NIHR | National Institute for Health Research |
| NMF | New Medicines Fund (Scotland) |
| NOCRI | NIHR Office for Clinical Research Infrastructure |
| NPAF | New Product Assessment Form |
| NSS | National Services Scotland |
| OMA | NICE Office for Market Access |
| OWMAG | One Wales Medicines Advisory Group |
| PACE | Patient and Clinician Engagement |
| PACS | Peer Approved Clinical System (Scotland) |
| PAS | Patient Access Scheme |
| PASAG | Patient Access Scheme Assessment Group (Scotland) |
| PASLU | Patient Access Scheme Liaison Unit |
| PASS | Post-Authorisation Safety Studies |
| PIC/S | Pharmaceutical Inspection Co-operation Scheme |
| PIL | Patient Information Leaflet |
| PIM | Promising Innovative Medicine |
| PIP | Paediatric Investigational Plan |
| PPI | Patient and Public Involvement |
| PREMs | Patient Reported Experience Measures |
| PROMs | Patient Reported Outcome Measures |
| PSMF | Pharmacovigilance System Master File |



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| Acronym | Name |
|---|---|
| QC | Quality Control |
| QMS | Quality Management System |
| RASRM | Regulatory Advice Service for Regenerative Medicine |
| REC | Research Ethics Committee |
| RMP | Risk Management Plans |
| RWD | Real World Data |
| SAE | Safety and Adverse Event |
| sCTMP | somatic Cell Therapy Medicinal Product |
| SMC | Scottish Medicines Consortium |
| SmPC | Summary of medicinal Product Characteristics |
| SPS | Specialist Pharmacy Services |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |
| TA | Technology Appraisal |
| TDP | Target Development Profile |
| TEP | Tissue Engineered Product |
| TGA | Therapeutic Goods Administration |
| TOPS | The Over-Volunteering Prevention System |
| UKCA | United Kingdom Conformity Assessed |
| USM | Urgent Safety Measures |
| WHSSC | Welsh Health Specialised Services Committee |



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