

Cell and Gene Therapy Catapult clinical trials database

Executive summary

The number of cell and gene therapy clinical trials in the UK continues to increase with 85 ongoing trials at present, representing a 37% increase over last year. For the first time the majority of trials have commercial sponsors, many of whom are non-UK companies. There has also been an increase in the proportion of gene modified therapies in clinical trial (73% in 2018 from 47% in 2017) with a number of *in vivo* therapies entering PhIII. The majority of these therapies use viral vector mediated gene delivery and there are now three trials employing gene editing technologies, CRISPR and TALEN for *ex vivo* modification and zinc finger nuclease for an *in vivo* application. Significant gene editing activity has also been identified in [Cell and Gene Therapy \(CGT\) Catapult preclinical database](#), therefore we anticipate the number of clinical trials to increase still further in the coming years.

Together these demonstrate the appeal of the UK for cell and gene therapy development work and clinical trials. This nurturing ecosystem has recently been developed still further by the establishment of the [Advanced Therapy Treatment Centre Network](#), funded by the UK government Industrial Strategy Challenge Fund. This network aims to build systems within the NHS to ensure that products progress effectively through clinical development and then commercialised in the UK.

Introduction to the database

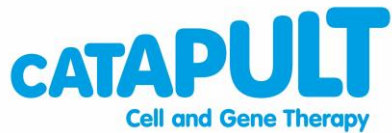
The UK Clinical Trials Database covers cell and gene therapy clinical trial activities that the CGT Catapult believes to be ongoing in the UK as of November 2018. It supersedes the database of July 2017, and both are available on our website.

The database has been compiled and verified by the CGT Catapult team, and includes:

- academic and commercial trials,
- ongoing trials in the UK, regardless of the nationality of the Sponsor,
- all trials involving cells as therapeutic agents*, and
- all trials involving *in vivo* and *ex vivo* gene therapy.

*excluding trials of haematopoietic stem cell transplantation regimens

The database is updated annually and provides what we believe to be a comprehensive and accurate review of the UK cell and gene therapy clinical trial landscape as of November 2018. The data presented here was collected between end of April 2017 and beginning of November 2018. The input of the cell and gene therapy community is important to help us maintain its relevance, and we welcome your updates, additions and corrections, which you can send to us at clinicaldatabase@ct.catapult.org.uk



The purpose of the CGT Catapult clinical trials database

As a centre of translational excellence in the UK, the CGT Catapult collaborates on and progresses a portfolio of therapeutic projects and related enabling technologies with the UK and international community. The clinical trials database forms an important part of the mechanism by which the CGT Catapult provides a highly relevant measure of progress in the field. Importantly, the database should provide a platform for use by academics, researchers and commercial organisations operating in the cell and gene therapy space to understand the extent of cell and gene therapy activities in the UK and to identify potential partners and collaborators.

It is complemented by the [preclinical research database](#) which covers cell and gene therapy projects ranging from early-stage translational research to late-stage preclinical development. This enables us to track trends, make predictions about clinical development and plan strategically.

Commentary on key findings 2018

The UK's portfolio of cell and gene therapy clinical trials is growing

The 2018 clinical trials database shows that there are 85 cell and gene therapy clinical trials ongoing in the UK. The majority of trials are in the recruitment phase, according to the information in the CGT Catapult database for which approval and verification was available. Four studies from the 2017 database have been completed and four have been suspended.

In 2017, we reported 62 cell and gene therapy clinical trials ongoing in the UK and this has been part of an ongoing trend of sector growth (Figure 1). Overall there has been a net increase in the number of new and ongoing trials compared to previous years, with a large amount of new trials and an increasing amount of gene therapy trials.

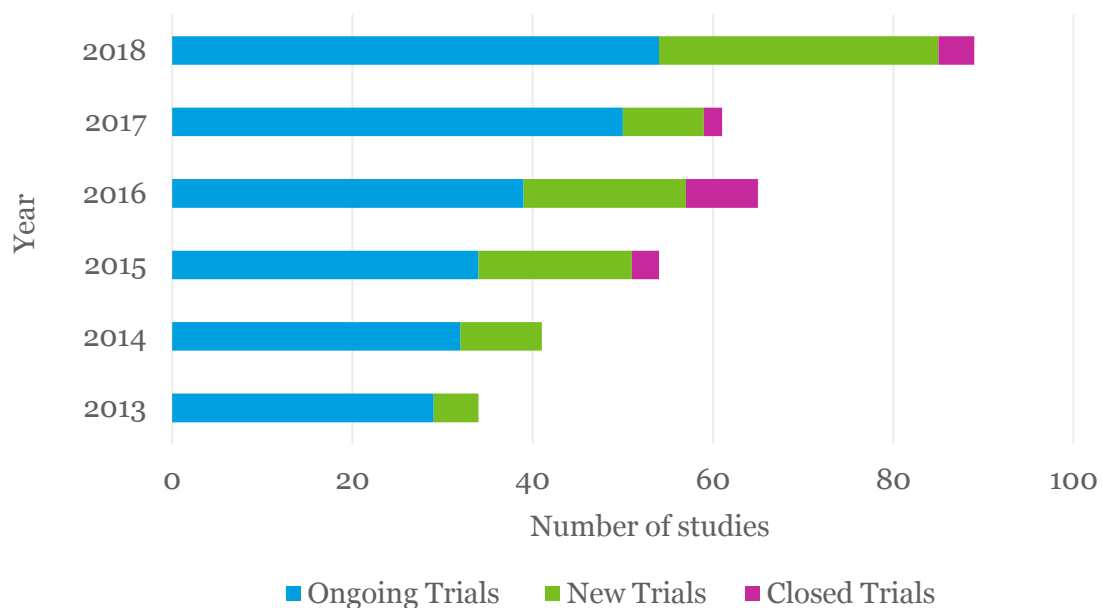


Figure 1. Number of ongoing, new and completed cell and gene therapy clinical trials in the UK from 2013-2018.

Majority of UK cell and gene therapy trials in recruitment phase

The majority of UK cell and gene therapy clinical trials are in the recruitment stage, as shown in the graph below (Figure 2). In 2018, the data shows that the number of trials currently recruiting has increased. The number of trials in planning has decreased since 2017, which is due to the increase in the number of trials moving from planning and into set-up and recruitment. There has also been an increase in the number of completed trials and trials that have been suspended. Overall, the data shows the progression of the portfolio, indicating that an increased number of subjects have been treated with cell and gene-based therapies in the UK.

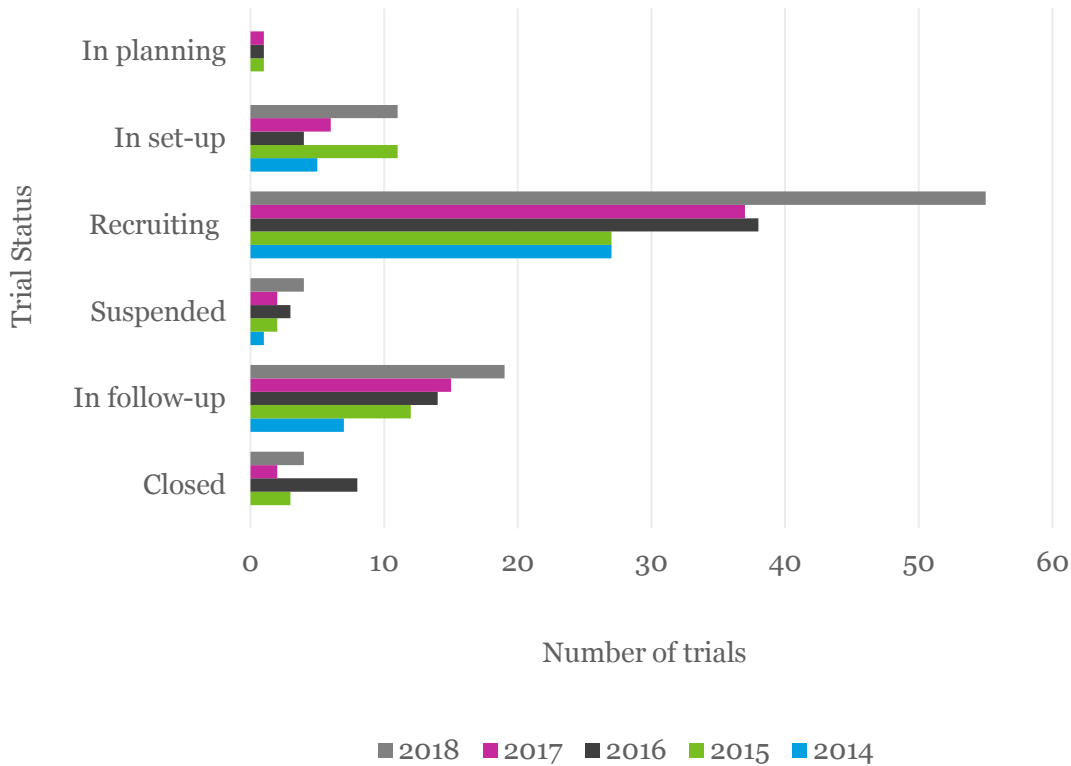


Figure 2. Distribution of UK clinical trials according to trial status from 2014-2018. (Data for 2013 not available)

Oncology indications remain the largest sector

Oncology, which includes haematological malignancies and solid tumours, remains the dominant therapeutic area (29%) as reported in previous years. Haematology (16%) is the second main therapeutic sector, followed by Ophthalmology (14%) (Figure 3).

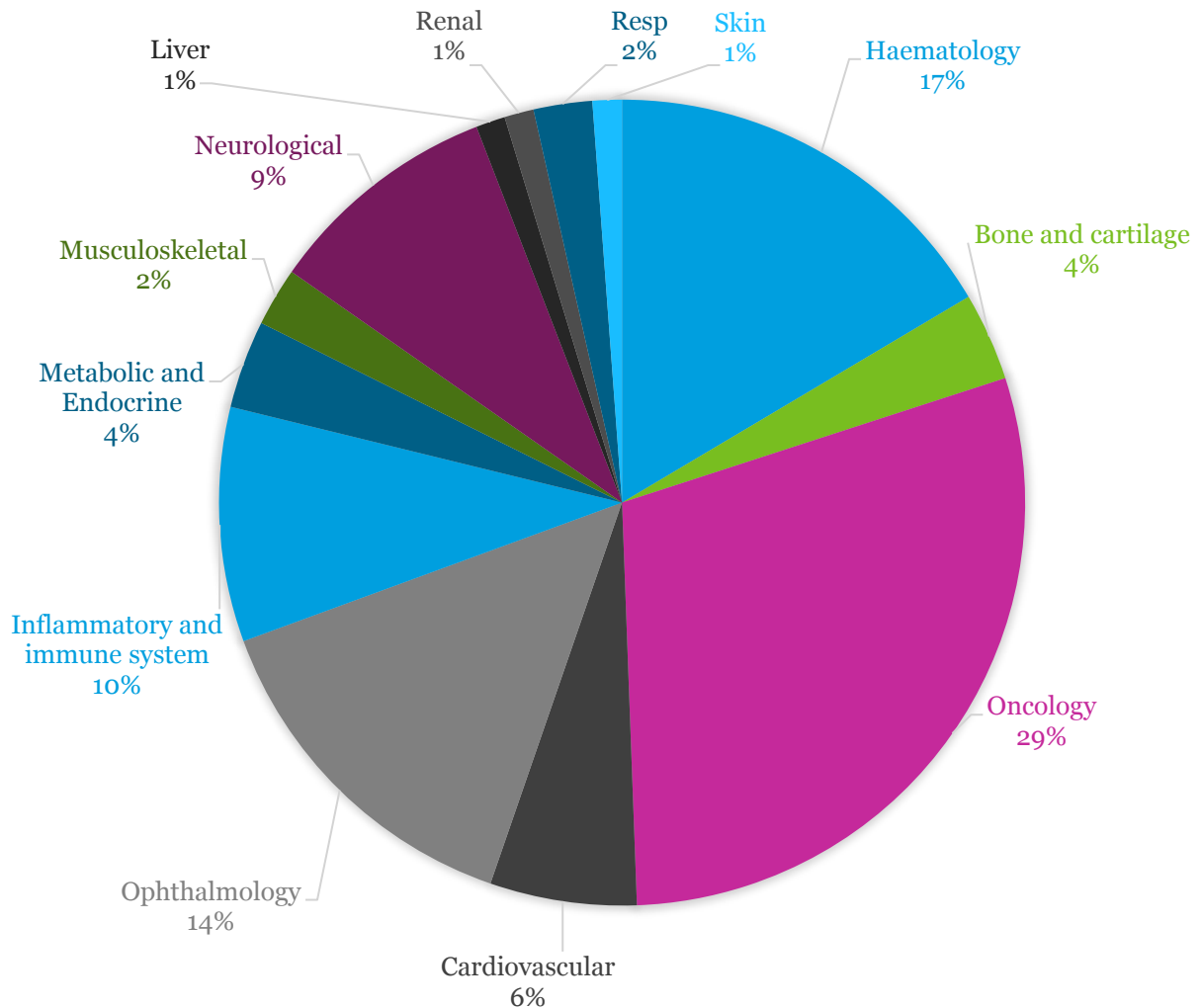


Figure 3. Distribution of UK cell and gene therapy clinical trials according to therapeutic area in 2018.

Diverse cell types with T cells and bone marrow-derived cells predominant

For cell-based therapies, the diversity of cell types in development is still reflected in this year's database. T cells (41%), CD34+ and/or CD133+ stem cells (18%) and mesenchymal stem/stromal cells (14%) continue to be the predominant cell types used in the clinic (Figure 4), followed by other immune cells (11%) and neural cells (7%). 'Other' contains various cell types which only feature in one or two trials.

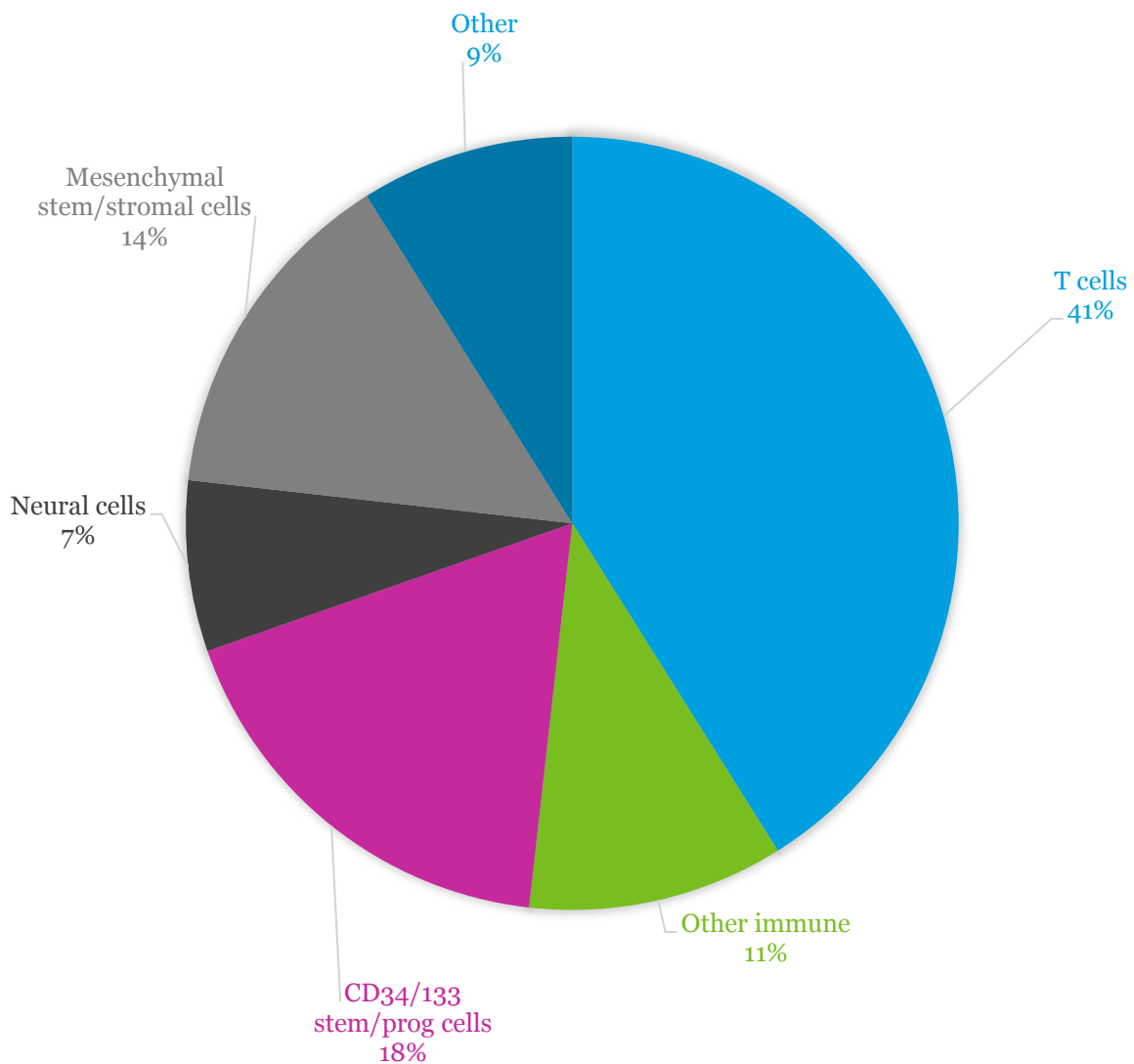


Figure 4. Breakdown of UK cell and gene therapy clinical trials by cell type in 2018.

Split between autologous and allogeneic in 2018

Autologous cell products are more frequently used than allogeneic products (2:1 ratio), and this has remained relatively constant as a ratio over the past six years (Figure 5).

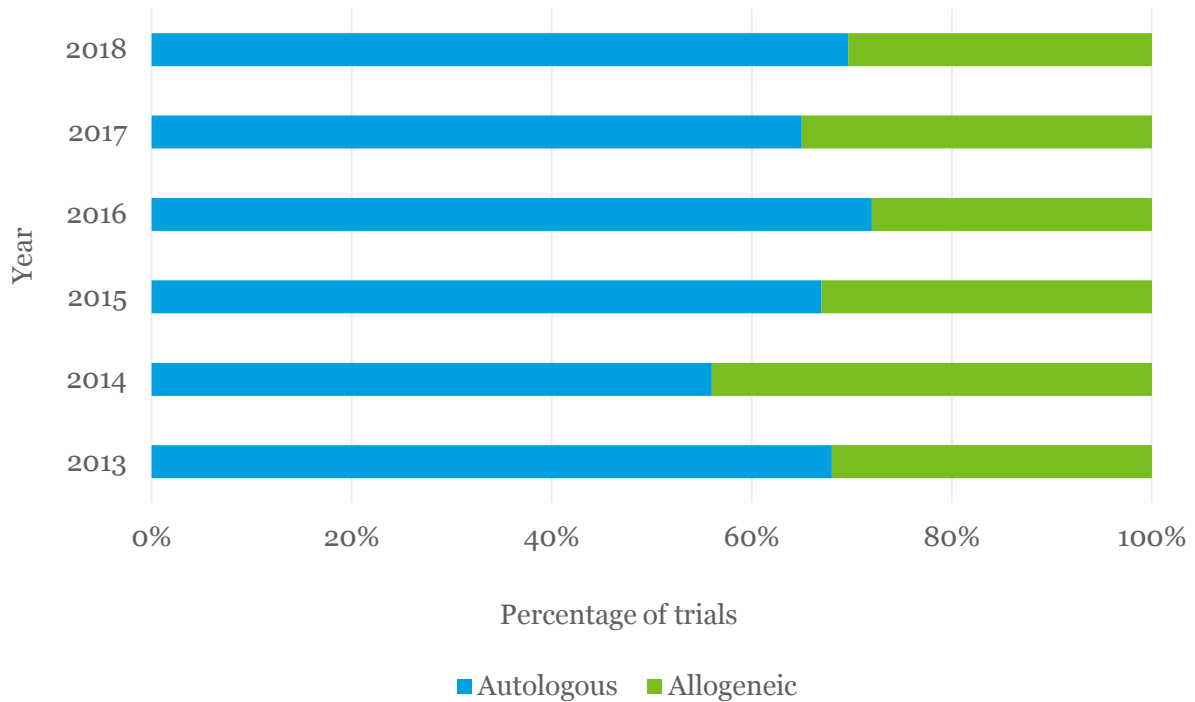


Figure 5. Distribution of autologous and allogeneic cell therapies in the UK clinical trials database from 2013-2018.

The majority of therapies are in early phase trials

The number of trials in phase I has remained fairly constant from 2017 to 2018 however a large increase is observed in PhI/II in 2018. There has also been a spike in PhIII trials in 2018 demonstrating progression of some products through clinical development, approximately 70% of these are in vivo gene therapy products (Figure 6). However, the majority of trials are at early phases with ~80% in PhI, PhI/II and PhII.

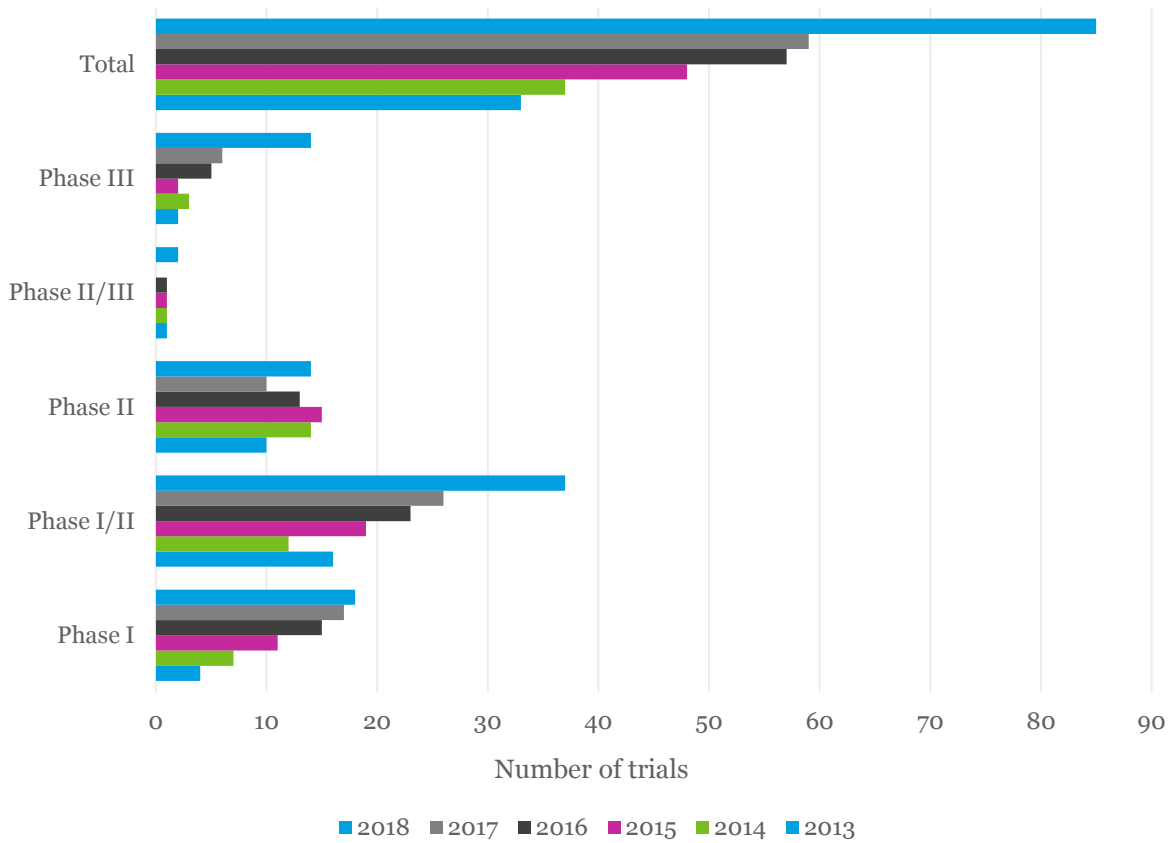


Figure 6. Cell and gene therapy clinical trials in the UK by clinical phase from 2013-2018 (2013 to 2016 figures show cell therapies only).

Growing numbers of UK clinical trials are sponsored by a commercial organisation

The number of commercially-sponsored clinical trials has increased in 2018 (Figure 7), likely reflecting the growing confidence in the cell and gene therapy industry attracting private companies and indeed a significant increase in UK spinouts over the past 12 – 18 months. Trials sponsored by a commercial sponsor have now become the majority in 2018 (66%). Of the 56 commercially sponsored trials, approximately one third are backed by UK companies with the remainder from outside the UK, US companies are well represented.

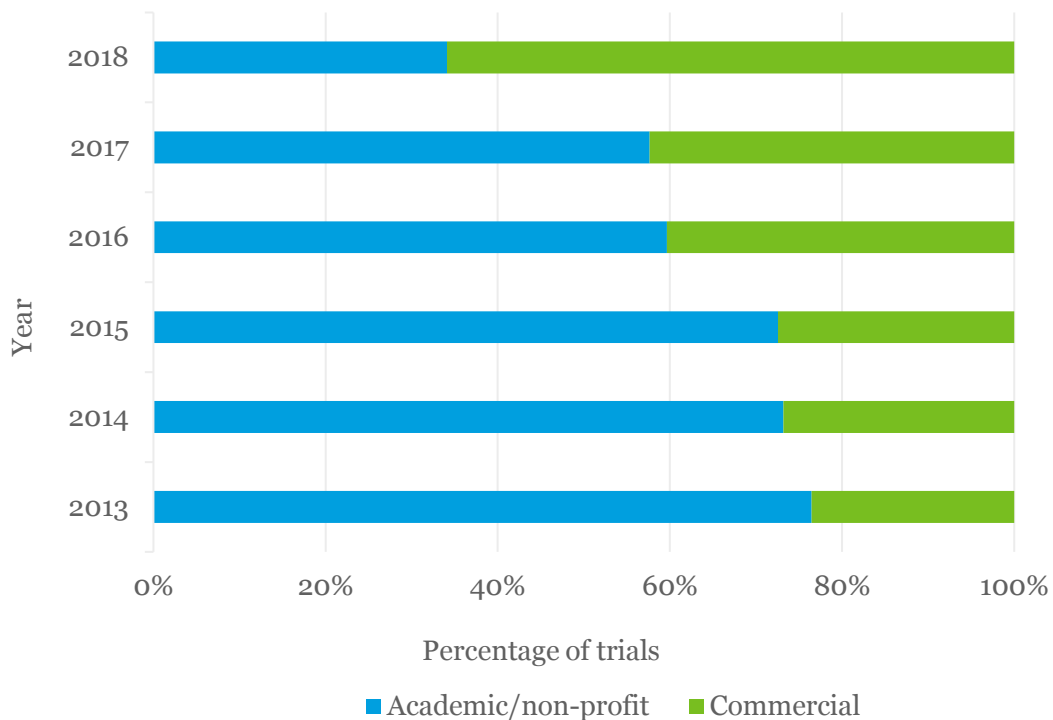


Figure 7. Proportion of commercial and academic/non-profit trial sponsors from 2013-2018.

Majority of therapies in the database are genetically modified (GM)

The 2018 database shows that ~70% of the clinical trials in the UK involve genetic modification (both *in vivo* and *ex vivo*) with the remaining ~30% using non-modified cells. The GM trials are split fairly evenly between *in vivo* and *ex vivo* modalities, 47% and 53% respectively (Figure 8a). There has been a significant increase in the use of adeno-associated virus (AAV) vectors (40% of gene modified trials) in comparison to 2017 (14% of gene therapy trials) reflecting the increase in *in vivo* therapies in trial. The use of gene delivery technologies is markedly different between *in vivo* and *ex vivo* applications as shown in Figure 8b.

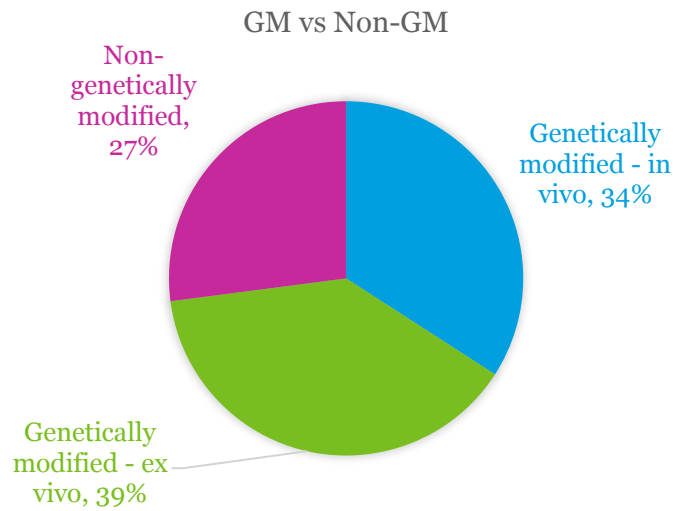


Figure 8a: Genetically modified therapies vs Non-Genetically Modified therapies in the UK - 2018

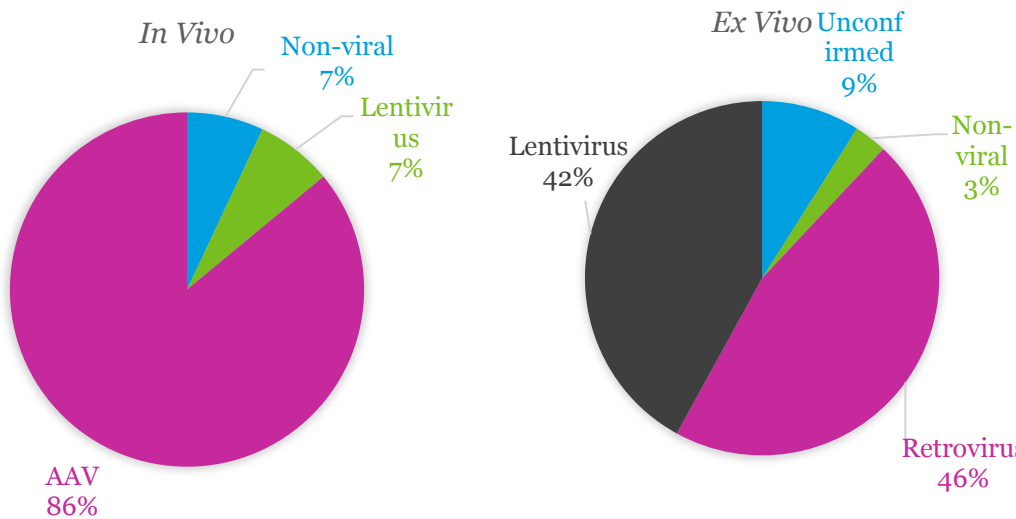


Figure 8b. Distribution of gene delivery technologies. Demonstrates clear split between non-integrating and integrating delivery between in vivo and ex vivo applications respectively

***In vivo* gene therapy landscape**

The 2018 database includes clinical trials of *in vivo gene* therapies which have been identified as currently ongoing in the UK. A total of 29 trials have been identified, of which 24 are commercially-sponsored: 20 are actively recruiting, six are in set up and three are in follow-up. As shown in Figure 8b above, the majority of trials utilise AAV vectors (86%) with 7% using lentiviral delivery and 7% using non-viral methods namely liposomes and antisense oligonucleotides. The *in vivo* gene therapy landscape is changing and growing and we welcome additional information from developers to add to the completeness of our databases.

The emergence of genome editing

Our analysis has identified three trials using genome editing technologies, although this is small in percentage terms, it demonstrates a significant step in the development of these technologies. The trials represent the three main approaches to genome editing with CRISPR and TALEN being used for *ex vivo* modification of hematopoietic stem cells (HSCs) and T cells respectively and a zinc finger nuclease approach being used for *in vivo* insertion of factor IX (FIX) to treat Haemophilia B. Demonstration of the efficacy of genome editing techniques may drive an increase in non-viral gene delivery as the requirement for viral integration for long-term expression of therapeutic genes is bypassed and more sophisticated gene correction becomes possible. An increase in activity in the genome editing space has been identified in our pre-clinical landscape review and is expected to result in an increased presence in the clinical trials database.

CGT Catapult clinical trials database – 2018 conclusions

The CGT Catapult's database of UK clinical trial activity reveals an industry that is growing and maturing with increasing numbers of companies involved in development of therapies and increasing numbers of clinical trials in recruitment or reaching completion. The majority of commercially sponsored trials are backed by non-UK based companies demonstrating the appeal of the UK for these types of trials due to the regulatory environment and scientific and clinical expertise available.

In 2016, *in vivo* gene therapy trials were included in the database for the first time and since then the number of *in vivo* gene therapy trials has increased from six to 29. This demonstrates growth and increased investment in this sector therefore, we expect to see continuous growth in years to come.

As well as providing CGT Catapult with important information on industry progress, we hope this database serves the cell and gene therapy community as a resource for planning future clinical programmes. For example, knowledge of which UK hospitals have experience in cell and gene therapies for specific therapeutic areas, or in the use of a certain cell type, as well as of which sponsors are supporting the cell and gene therapy area can be important information in clinical trial planning and the search for potential funding.