The Cell and Gene Therapy Catapult UK clinical trials database

The UK clinical trials database covers cell and gene therapy clinical trial activities that the Cell and Gene Therapy Catapult (CGT Catapult) believes to be ongoing in the UK as of June 2017. It supersedes the database of July 2016, 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*
- 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 the most comprehensive and accurate review of the UK cell and gene therapy clinical trial landscape as of June 2017. The data presented here were collected between end of March 2016 and beginning of May 2017. 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 UK 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 UK clinical trials database forms an important part of the mechanism by which the CGT Catapult identifies potential programmes for investment or partnership, and 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/collaborators.

It is complemented by a UK Preclinical Research Database, also available on our website, 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

1) The UK's portfolio of cell and gene therapy clinical trials is progressing

The 2017 clinical trials database shows there are 59 trials in cell and gene therapy 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.

We believe 9 of the 59 ongoing cell and gene therapy trials in the 2017 database to be new to the database, none of which have progressed from the pre-clinical database. Two studies from the 2016 database have been completed and two have been suspended.

In 2016, we reported 57 cell and gene therapy clinical trials ongoing in the UK and this has been part of a trend of growing numbers of ongoing clinical trials in the sector (**Figure 1**). This year, the number of trials to be completed has decreased however, overall there has been a net increase in the number of ongoing trials compared to previous years.

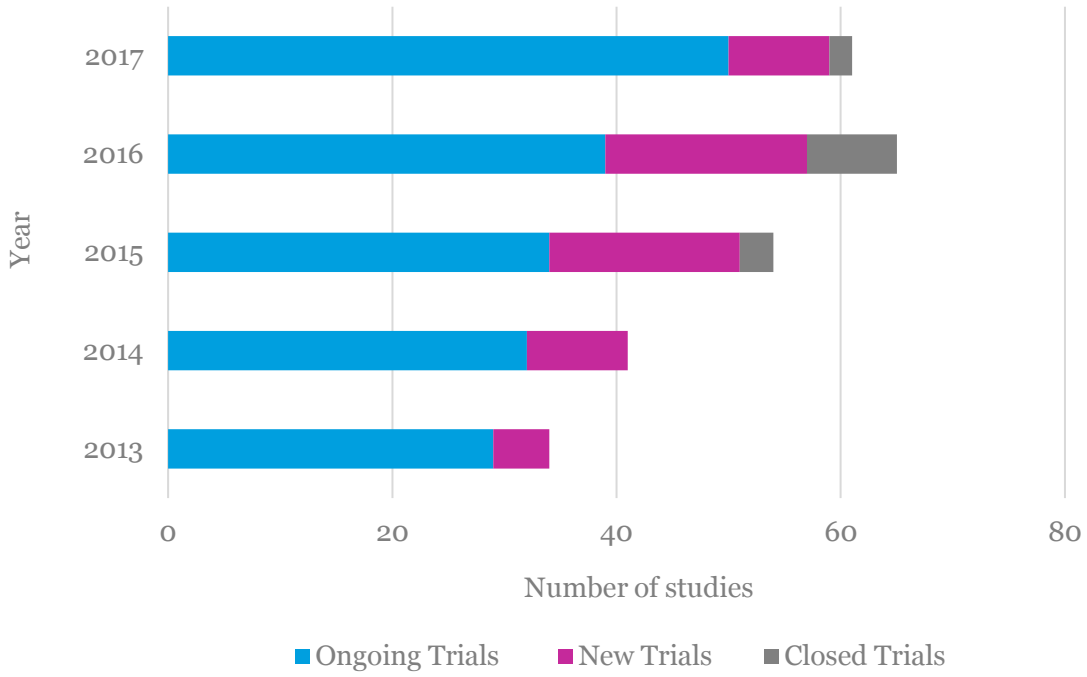

Figure 1. Number of ongoing, new and completed cell and gene therapy clinical trials in the UK from 2013-2017.

2) 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 2017, the data shows that the number of trials currently recruiting has decreased, however this was only by one trial. The number of trials in planning has not changed since 2016, however the number of trials in set-up and in follow up has increased. There has been a decrease in the number of completed trials and trials that have been suspended. Overall, the data shows the progression of the portfolio, meaning that an increased number of subjects have been treated with cell and gene based therapies in the UK.

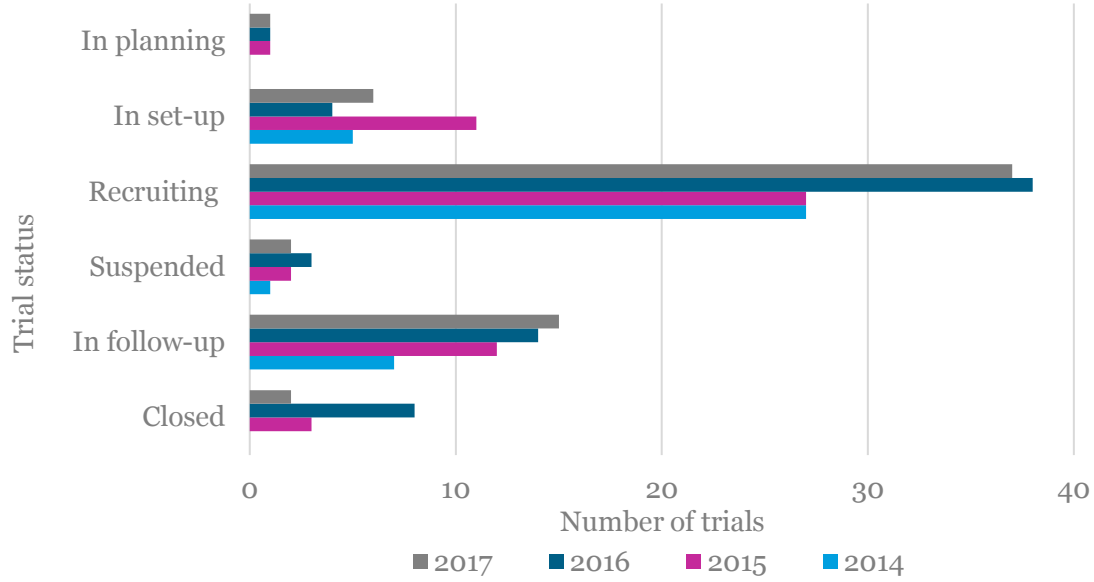

Figure 2. Distribution of UK clinical trials according to trial status from 2014-2017. (Data for 2013 not available)

3) Oncology indications remain the largest sector

Oncology, which includes haematological malignancies and solid tumours, remains the dominant therapeutic area (20%) as reported in previous years. Ophthalmology (14%) is the second main therapeutic sector, followed by Neurology (13%) (**Figure 3**).

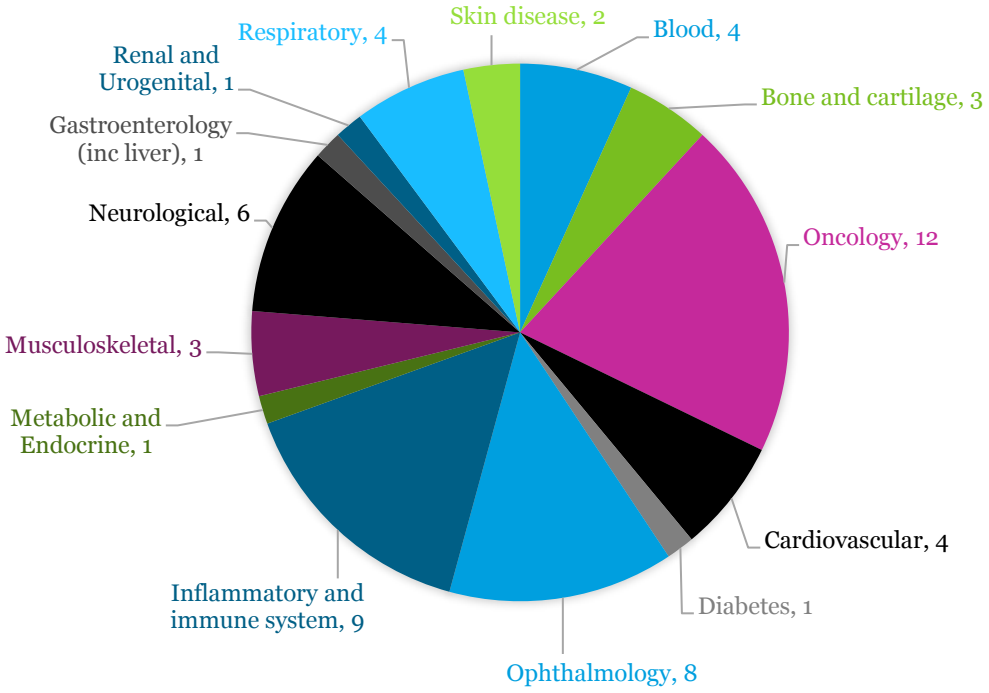

Figure 3. Distribution of UK cell and gene therapy clinical trials according to therapeutic area in 2017

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

For cell based therapies, the diversity of cell types in development is still reflected in this year's database. T cells (14 trials, 29%), CD34+ and/or CD133+ stem cells (8 trials, 17%) and mesenchymal stem/stromal cells (8 trials, 17%) continue to be the predominant cell types used in the clinic (**Figure 4**), followed by neural cells (5 trials, 10%) and bone marrow mononuclear cells (3 trials, 6%).

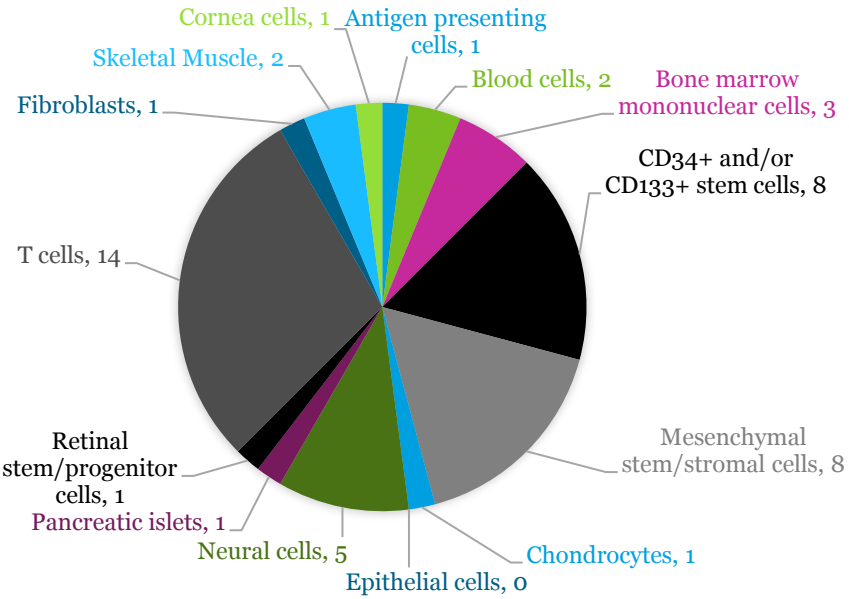

Figure 4. Breakdown of UK cell and gene therapy clinical trials by cell type in 2017.

5) Split between autologous and allogeneic 2:1 in 2017

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 four years. The trend from 2014 to 2016 showed an increase in autologous cell products. In 2017 however, there has been a change in this trend with the number of allogeneic cell products increasing and number of autologous cell products decreasing. (**Figure 5**).

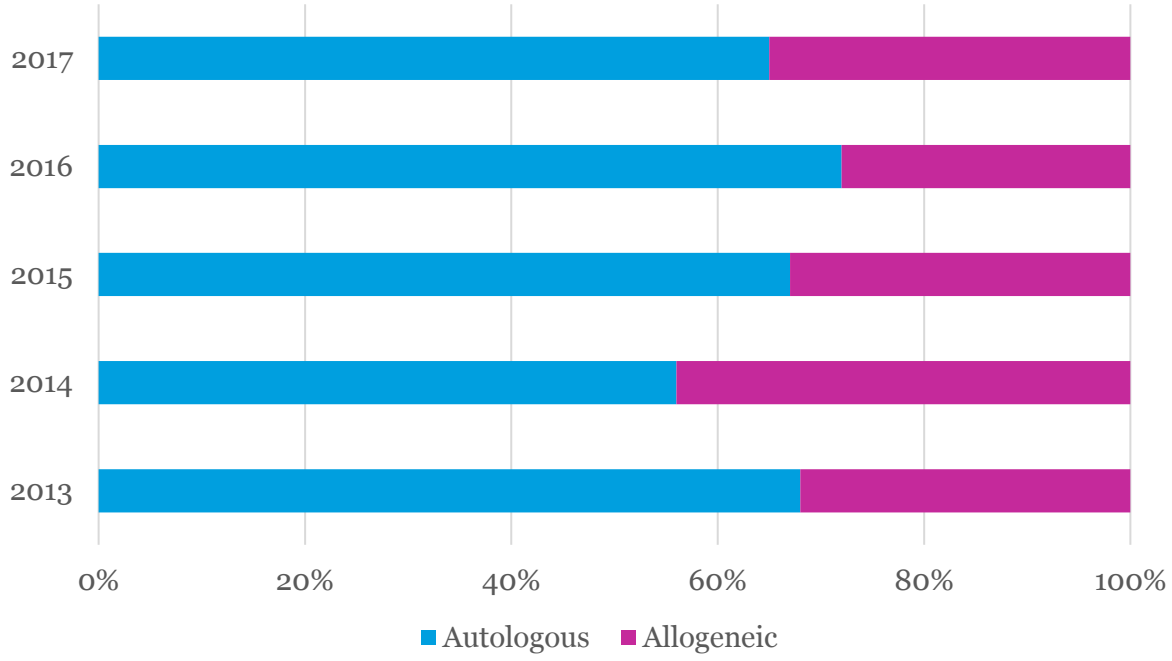

Figure 5. Distribution of autologous and allogeneic cell therapies in the UK clinical trials database from 2013-2017.

6) The majority of therapies are in early phase trials

There has been a steady increase in the number of trials in phase I and phase I/II as new entities enter development. Therapies previously at Phase II progress to Phase III (**Figure 7**). However, whilst there has been an increase in the number of Phase III trials in 2017, the UK portfolio of activity remains at an early phase with still relatively few therapies in Phase II/III or Phase III.

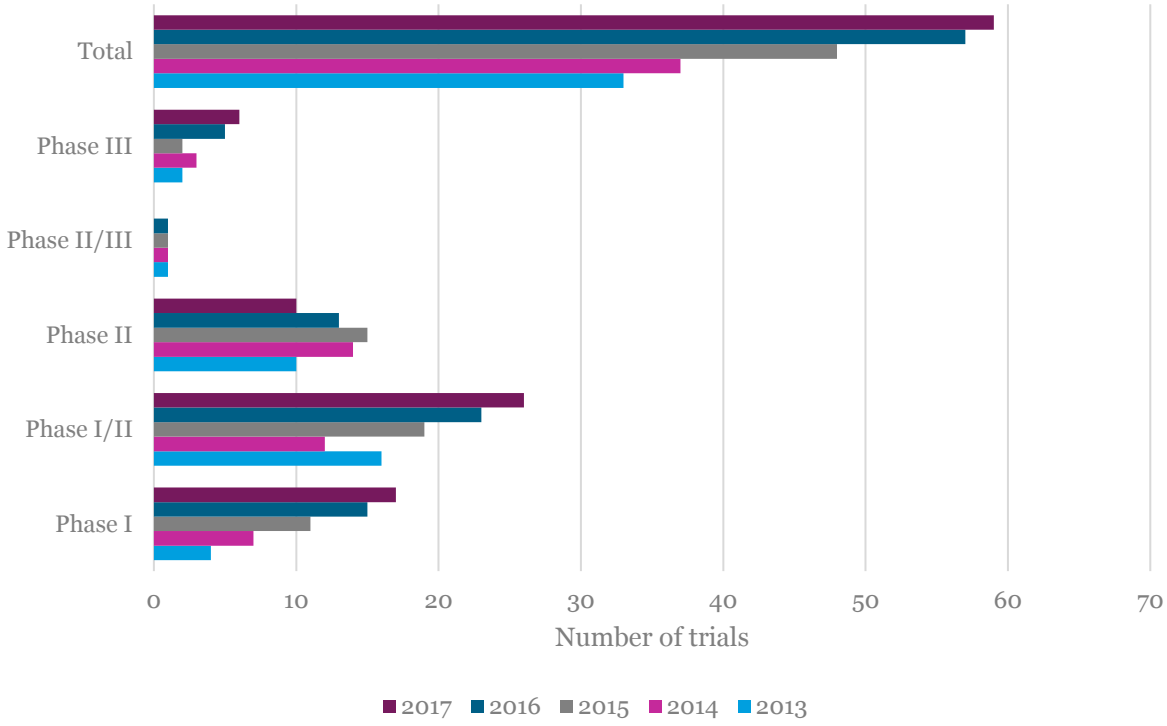

Figure 7. Cell therapy clinical trials in the UK by clinical phase from 2013-2017 (2017 figures also show the total for cell and gene therapies combined).

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

The number of commercially-sponsored clinical trials has increased in 2017 (Figure 8), 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 academic and research institutions remain the majority (58%).

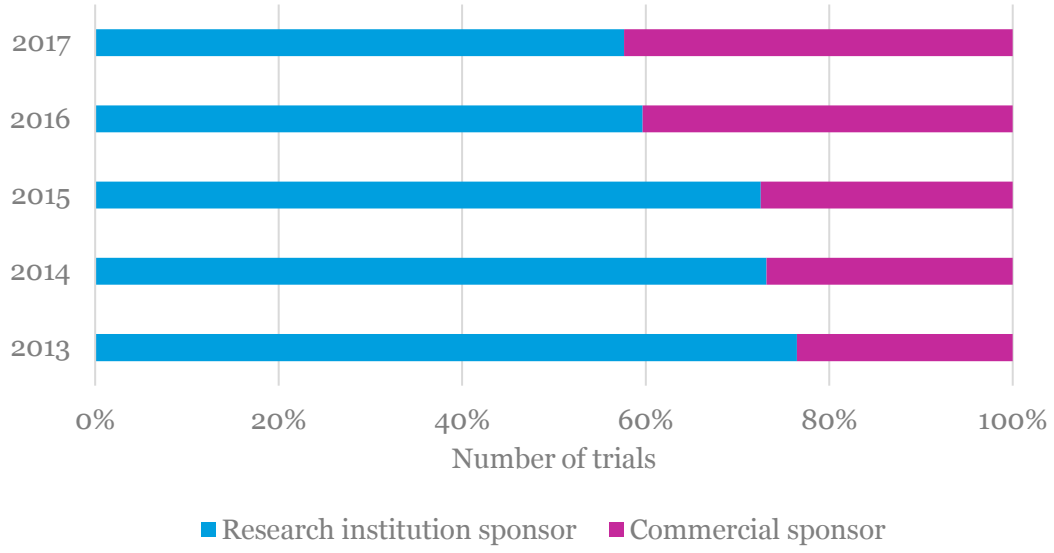

Figure 8. Proportion of commercial and research institution trial sponsors from 2013-2017.

8) Majority of therapies in the database are non-genetically modified

The 2017 database shows that 53% of cell and gene therapies currently used in clinical trials in the UK do not involve genetic modification. The remaining 47% of trials involve cell and gene therapies modified *ex-vivo* with a vector or *in vivo* gene therapies, the majority of which use a lentiviral-based vector (**Figure 6**). There has been a significant increase in the use of AAV vectors (14% of gene therapy trials) in comparison to 2016 (7% of gene therapy trials).

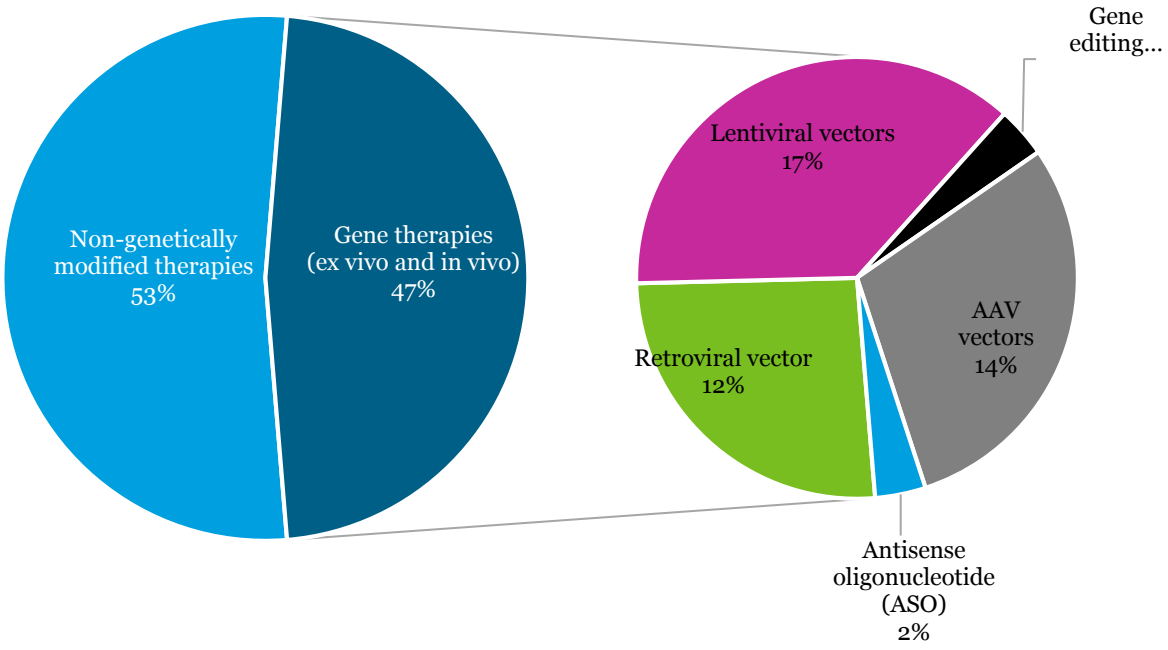

Figure 6. Genetically modified cell therapies used in UK clinical trials in 2017.

9) *In vivo* gene therapy landscape

The 2017 database includes clinical trials of *in vivo* gene therapy which have been reported to us as currently ongoing in the UK. A total of 10 trials have been identified, of which 7 are commercially-sponsored. Six trials are in the recruiting phase, 3 in follow-up, and 1 in set-up. In terms of vector type, the majority of trials use an AAV vector (8) and only 1 a lentiviral-based vector. The database also includes one trial of antisense therapy using a single stranded antisense oligonucleotide designed to reduce the production of the huntingtin (HTT) protein, which is the genetic cause of Huntington's disease (HD). 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.

10) Database utility for developers

As well as providing the CGT Catapult with important information on industry progress, the database should serve 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 search for potential funding.

11) UK cell and gene therapy clinical trials database – 2017 conclusions

The CGT Catapult's database of UK clinical trial activity reveals an industry that is growing and maturing in the UK with increasing numbers of companies involved in development of therapies and increasing numbers of clinical trials in recruitment or reaching completion. In 2016, *in vivo* gene therapy trials were included in the database and since then the number of *in vivo* gene therapy trials have increased from 6 to 10. This demonstrates growth and increased investment in this sector therefore, we expect to see continuous growth in years to come.

We hope that cell and gene therapy researchers and organisations will find our UK clinical trials database informative and useful. As the CGT Catapult and others focus on translational activities, we expect the analyses of future years to show an industry undergoing significant growth and moving towards maturation.