BREXIT: the impact on medical innovation and patients in the UK

When your child is diagnosed with a cruel and terminal disease, your thoughts turn immediately to the research: what's going on, who can I turn to, where can I get my child onto a clinical trial? In the UK we are privileged to benefit from access to some of the world's leading academic and health institutions, often pioneers in ground breaking research that is saving lives.

Brexit has the very real potential to cut off our ability to access these opportunities, with devastating repercussions on research and medical advances: This isn't a matter of playing politics; it's a matter of saving lives.

This short document lays out the benefits of EU collaboration, using Duchenne Muscular Dystrophy (DMD) as the case study.

Executive Summary

Duchenne UK has compiled this document to highlight the benefits of EU collaboration to our community; to patients, scientists and industry.

The very nature of rare disease, small patient populations geographically spread out with scarce and scattered resources and expertise, means the Duchenne Muscular Dystrophy (DMD) community has been uniquely placed to benefit from EU collaboration, crossing borders, uniting communities. National funding streams have not historically prioritised funding research outside their borders - and patients suffer. We cannot return to that model.

In 5 years, more than **€22million** has been invested in DMD research through the EU's FP7 and Horizon 2020 programmes.

Patients are currently participating in potentially life saving trials in the UK, because of EU funding.

Our paper, '**Brexit: the impact on medical innovation and patients in the UK'**, uses real-life illustrations of the impact of Brexit already felt and imminently expected. We have gathered testimony from patients and families living with Duchenne, CEOs from pharma already running trials, clinicians treating patients and key players in cutting-edge research into new therapies for Duchenne.

We ask that the government understands that UK membership of the EU and access to its innovation platforms, is fundamental to the growth of a scientific and medically driven knowledge-based economy that is the future of wealth creation in this country.

We ask that our status and access to EU funding is preserved, because this model is particularly effective in rare disease. We urge the government to fill any funding voids with immediate loans, and address the problems of scientists being dissuaded from applying for EU grants because of the UK's current status.

We ask that the UK's participation in EU programmes such as Horizon 2020 remains, and we are guaranteed - at the minimum - associated membership, according to Article 7 of the H2020 EU Directive, in a form similar to other non-EU member countries like Norway and Israel. European wide funding streams accelerated and enhance research, opening up more opportunities for patients, in a away that national funding streams and projects do not.

As Professor Katie Bushby says in our document
"We risk a long time in the wilderness"

"Brexit will likely have a direct impact on the participation of, and benefits received by, UK academic partners in such EU-funded research and policy projects. There is also concern for the loss of high level scientific expertise that comes from the UK."

Yann Le Cam, CEO, Eurordis

1. Losing EU Funding: the impact on research and clinical trials

The very nature of rare disease, small patient populations geographically spread out with scarce and scattered resources and expertise, means it is uniquely placed to benefit from EU collaboration, crossing borders, uniting communities. In 5 years, more than **€22million** has been invested in DMD research through the EU's FP7 and Horizon 2020 programmes, which, in total, invest **€150 billion** in research and innovation. Patients are currently participating in potentially life saving trials in the UK, because of EU funding.

- The SKIP-NMD exon skipping trial received **€5.6m** from FP7: 24 patients are now on trial for a drug, provided by Sarepta Therapeutics, that could alleviate symptoms in 13% of DMD sufferers

" We at Sarepta Therapeutics have appreciated the affiliation with the UK which allowed us to access other neuromuscular centres in Europe. We look at London as the gateway into Europe because it has such good research centres for neuromuscular disease both in London and in Newcastle, that have formed very strong pan-European collaborations for clinical trials and other research efforts. The FP7 grant enabled us to perform the first study for our SRP-4053 drug in Europe rather than the United States"

Edward M Kaye MD, Interim CEO & CMO, Sarepta Therapeutics

✦ The Vision DMD programme received **€8million** euros to fund a Phase II study of Vamorolone, a steroid alternative. The trial is being led by the team at Newcastle, and will have ten trial sites across the UK and Europe.

"EU grants are more than "just" the money. They offer the possibility for collaboration and international work which is essential if you are going to do research, especially in rare diseases. Our H2020 grant Vision DMD is a good example of this; it's enabling a trial which will involve several EU countries. Lack of sufficient numbers of patients in any one country means that rare disease trials almost always need to be international. Having access to a pot of money which encourages this is crucial - national funding streams simply do not have as a priority funding research outside their borders, a short sighted approach which disadvantages people with rare conditions.

As a member of the EU we had the potential to lead and influence across a broad stage. Sitting on the fringe means that others will make decisions and lead and (if we are lucky) we can get the crumbs from the master's table. This is a very sorry state of affairs for the UK to be in.

We risk a long time in the wilderness.

Professor Katie Bushby, Professor of Neuromuscular Genetics

Leaving the EU will put access to future funding in jeopardy. Patients will suffer, as research opportunities will be closed off to them.

" A clinical trial is the best chance I have of potentially saving my son's life. To see those opportunities being closed off to the UK is like torture. It's like we're on the Titanic: we can see the lifeboats that might get us to safety, but we're powerless. We know they can't reach us. And what makes it worse, is that it didn't have to be this way."

Divyesh Popat, whose son took part in an EU funded clinical trial for DMD

2. Academic Case Study: University College, London (UCL)

The Horizon 2020 grant is the EU's biggest Research and Innovation funding scheme, with **€79 billion** of funding available over seven years (2014 to 2020). This programme is entirely meritocratic; due to the high standards of UK academia the UK has managed to secure large sums in the past years, essential for driving medical research.

- In 2014 UCL's success rates of winning grants, was four times the EU average
- In 2015 UCL, together with Imperial College, received a total of **€129 million** in EU funding: That's more than all the French National Research Centres together (1100 research units)

"Biotech companies and pharma industries are highly invested in a partnership with academic institutions because of their important knowledge base and high research expertise and output.
The capacity of these academic institutions to take the lead in multi-national research networks, is an essential element of their attraction. Industry-derived funding is essential for developing and implementing new therapies, in particular for rare diseases. In EU countries progress has been accelerated through sharing of resources, knowledge, patient cohorts, and infrastructure in joined-up and integrated networks.
By breaking up the close research ties with EU partner states, the top performing UK academic institutions, who are a major motor for the development of new treatment approaches, risk losing out from EU financial support, networking capacity, access to early shared knowledge and access to comprehensive databases which are all indispensable assets for modern research.
The capacity of these academic institutions to take the lead in multi-national research networks, is an essential element of their attraction. Industry-derived funding is essential for developing and implementing new therapies, in particular for rare diseases. In EU countries progress has been accelerated through sharing of resources, knowledge, patient cohorts, and infrastructure in joined-up and integrated networks."

Joint Opinion, Dr. Valeria Ricotti, Honorary Clinical Lecturer, Institute of Child Health and GOSH, and Professor Thomas Voit,
Director Designate of NIHR GOSH UCL Biomedical Research Centre

3. Medical Centre Case Studies: Great Ormond Street Hospital, London and the John Walton Muscular Dystrophy Research Centre, Newcastle

The UK is internationally renowned for DMD research, because of two leading academic and medical institutions in the UK: Great Ormond Street Hospital in London, and The John Walton Muscular Dystrophy Research Centre in Newcastle.

Great Ormond Street Hospital

- At Great Ormond Street Hospital in London, **none of the FOUR consultants** working with Duchenne patients is originally from the UK.
- The Neuromuscular research team at GOSH has won **TEN** awards, and is currently running projects worth **€6.9 million**

"My group, via the EU Network, has identified 29 new disease genes. This is only due to the networking capacity and the ability to pull together ideas and expertise."

Professor Francesco Muntoni, The Dubovitz Neuromuscular Unit, Institute of Child Health and GOSH

John Walton Muscular Dystrophy Research Centre (JWMDRC)

- In Newcastle, 30% of the 90 staff members are from EU member states, providing vital care and research
- The JWMDRC has won **THIRTEEN** EU grants in 4 years. Newcastle University has received **€80 million**, with **€10 million** coming to the JWMDRC

"The outcome of the referendum was a very sad day for all rare disease patients in the UK, who benefit from research. A huge number of our successes in the last decade were based on fruitful and enjoyable collaborations with colleagues from the EU. Many translational research projects - projects that really matter to patients - have either been directly funded by the EU or by patient organisations from EU countries. A third of our 90-strong team are EU citizens able to work here freely because of our membership. More than €10 million of funding has come directly to these experts at Newcastle in just the last 4 years to fund their vital research into neuromuscular diseases."

Professor Volker Straub, JWMDRC, Newcaslte

White dots = Staff from the EU
Grey dots = staff funded by EU on rare disease research
Visible = mainly students & staff from the NHS

4. The European Medicines Agency (EMA) - Gateway to Europe

European Medicines Agency (EMA)

The EMA is currently located in Canary Wharf in London with a "mission to foster scientific excellence in the evaluation and supervision of medicines … in the European Union".

> 'The EU provides a single framework for regulating and improving pharmaceutical products. This ensures a high standard of patient safety, raises productivity through economies of scale and increased competition, and reduces the cost of supplying drugs across the EU. The UK has strong influence over the EU's regulatory framework for pharmaceuticals, which would be lost under any of the alternative relationships.'
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> UK Treasury Report

"Because of London's access to talent in the biotech field, and the access it affords to the EMA in Canary Wharf, we'd been planning to open our first European office in London in preparation for an MAA filing in November. With the exit of the UK from the EU, we will be forced to reconsider that plan; we feel the recent Brexit vote will hamper our ability to perform research and clinical trials in the UK and throughout Europe."

Edward M Kaye MD, Interim CEO & CMO, Sarepta Therapeutics

5. Investment in industry: Patients will suffer both from reduced access to clinical trials and delays in accessing new medicines

The UK is the EU's main destination for venture capital funding in these industries. Between 2005 and 2015, the UK's biotech sector raised £924m via initial public offerings and US $2.4 billion, in venture capital.

> "Pharma always has extremely strategic plans in place for the launch sequence of bringing new drugs to market. If market access in the UK no longer guarantees entrance to the EU market, then it could be viewed as being a much less attractive place to launch from and indeed to invest in. The UK's fragmented market access systems and reluctance to pay high prices could compound the situation making the UK a less attractive launch market and consequently less attractive as a place to do clinical trials."
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> UK BioIndustry Association

Any threat to this could directly impact the timing and availability of new treatments to patients in the UK.

""There are significant advantages in the development of new treatments, including ones for Duchenne muscular dystrophy, in the UK being part of the wider European regulatory regime for development of new medicines. Over many years, an effective and integrated European medicines framework supporting clinical research and development has been established and includes the UK's globally respected regulator, the MHRA. By being a key part of the framework, the UK receives substantial advantages by being able to have access to skilled developers and marketers of drugs, and also means the UK market is among the first to receive access to ground breaking-treatments. If the UK withdraws from the European framework, or if the EMA relocates away from London, there is a high risk to the UK retaining the skilled workforce that has been created, and the speed with which patients are able to gain access to lifesaving new medicines."

Glyn Edwards, CEO Summit Therapeutics

6. A way forward

Duchenne UK has compiled this document to highlight the benefits of EU collaboration to our community, and we urge those reading this to preserve and retain as much of this valuable collaboration as possible.

We ask that:

1. The government understands that UK membership of the EU and access to its innovation platforms, is fundamental to the growth of a scientific and medically driven knowledge-based economy that is the future of wealth creation in this country. And that as the Prime Minister, Theresa May has stated, life sciences is a core national industry priority.

2. That our status and access to EU funding is preserved, because this model is particularly effective in rare disease. We urge the government to fill any funding voids with immediate loans, and address the problems of scientists being dissuaded from applying for EU grants because of the UK's current status.

3. That EU national scientific staff and NHS staff have automatic resident status guaranteed for their contracts.

3. That the UK's participation in EU programmes such as Horizon 2020 remains, and we are guaranteed - at the minimum - associated membership, according to Article 7 of the H2020 EU Directive, in a form similar to other non-EU member countries like Norway and Israel. National funding streams do not prioritise funding research outsider their borders, a short-sighted approach which disadvantages patients with rare conditions.