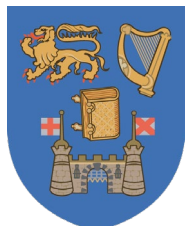


# St James's Hospital Wellcome - HRB Clinical Research Facility

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Prof. David Kevans  
Consultant Gastroenterologist, SJH  
Associate Director CRF



Wellcome - HRB  
**Clinical Research Facility**  
at St. James's Hospital





# SJH-Wellcome-HRB CRF Mission & Vision

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## **Mission**

To improve health outcomes by leading and enabling high quality, innovative patient-focused clinical research

## **Vision**

To accelerate experimental medicine research including access to and adoption of drugs, devices and diagnostic tests ensuring inclusivity across diverse patient populations, performing at a level comparable with the best international centers



# SJH-Wellcome-HRB CRF Management Team

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**Prof. M Hennessy**  
CRF Director / TCD



**Prof. E Vandenberghe**  
CRF Associate Director



**Prof. D Kevans**  
CRF Associate Director



**Dr. Cormac Kennedy**  
CRF Associate Director



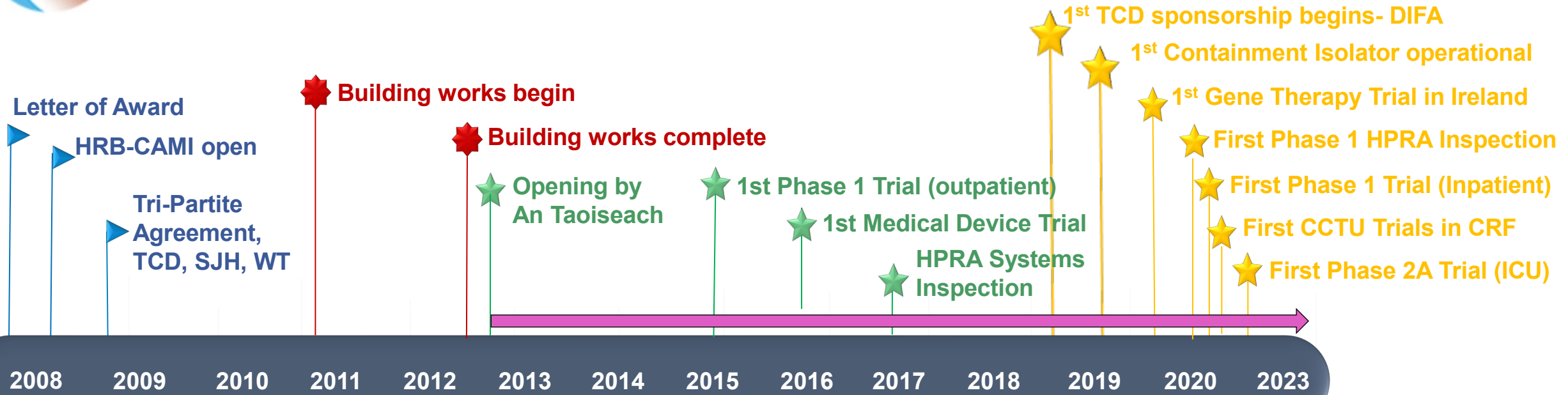
**D Reidy**  
CRF COO / ADON



**J Towns**  
Programme Manager



# SJH-Wellcome-HRB CRF Evolution



Prof. Kelleher

Prof. Gill

Prof. Hennessy

Prof. Bergin

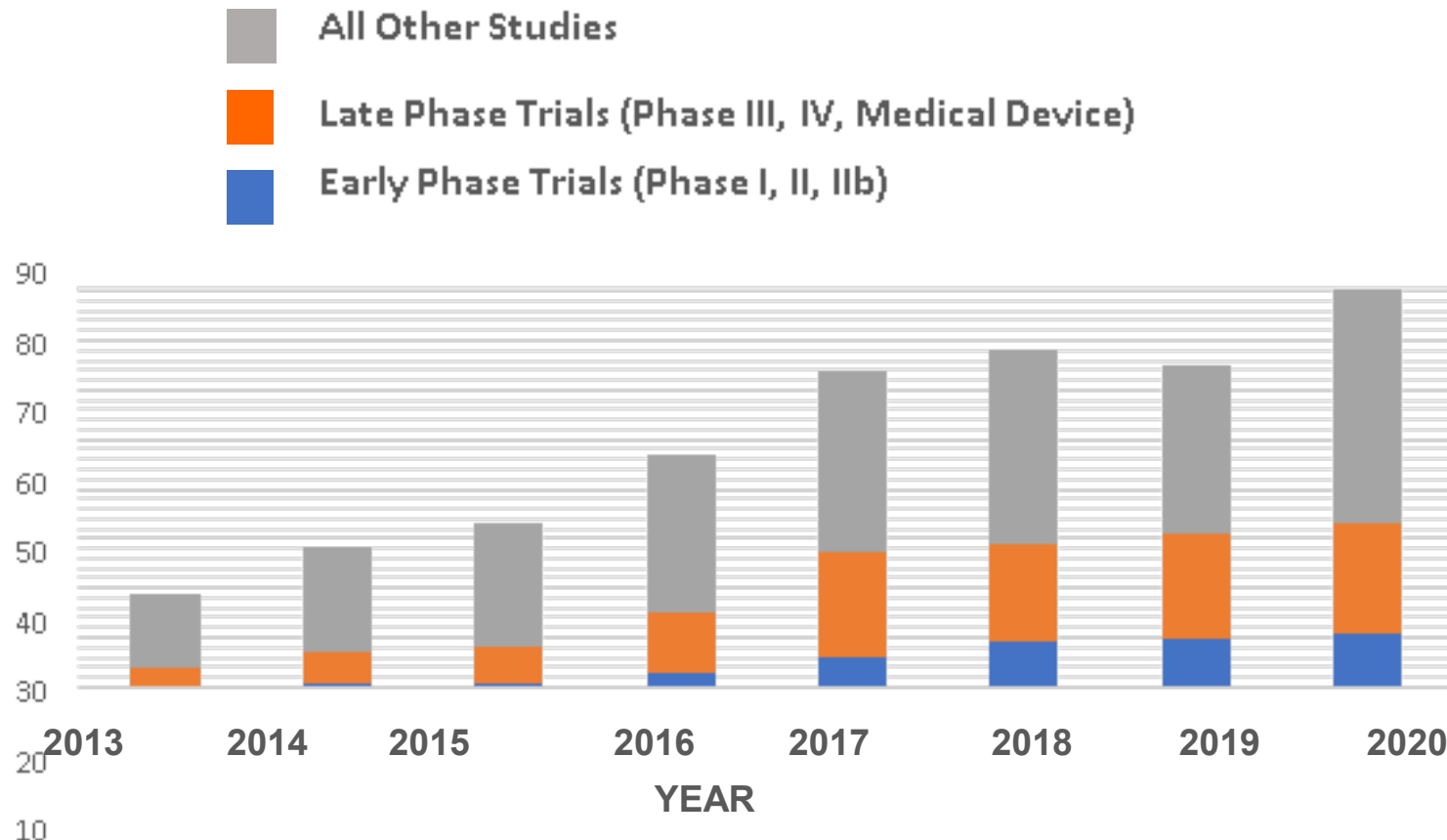
Prof. Kevans

Prof. Vandenberghe



# SJH-Wellcome-HRB Clinical Research Facility - Activity

Breakdown of Open CRF Clinical Trials/Studies by Type, 2013 to 2020



- Mean Study Intensity is 4.5 (UK-CRF study intensity tool)
- 19 studies at highest intensity level (6)
- 2.3 fold increase in participant visits outside core hours.

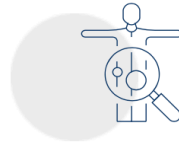


# SJH-Wellcome-HRB Clinical Research Facility - Activity

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## Our Impact

Since opening in May 2013, the CRF has grown from strength to strength supporting a wide variety of clinical trials and studies, more notably the CRF has successfully conducted the first gene therapy clinical trial in haemophilia in Ireland along with a Phase 1 overnight clinical trial in neurology.



Disease Areas

**19**

St. James's Hospital is Ireland's largest acute academic teaching hospital. We support a wide range of studies in multiple disease areas.

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Investigators

**105**

We collaborate with a wide range of investigators across a variety of disease spectrums.

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Regulated Clinical Trials

**76**

This includes early Phase I /II to Phase III and medical device studies.

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Non-Regulated Clinical Studies

**137**

This includes observational studies and interventional studies.

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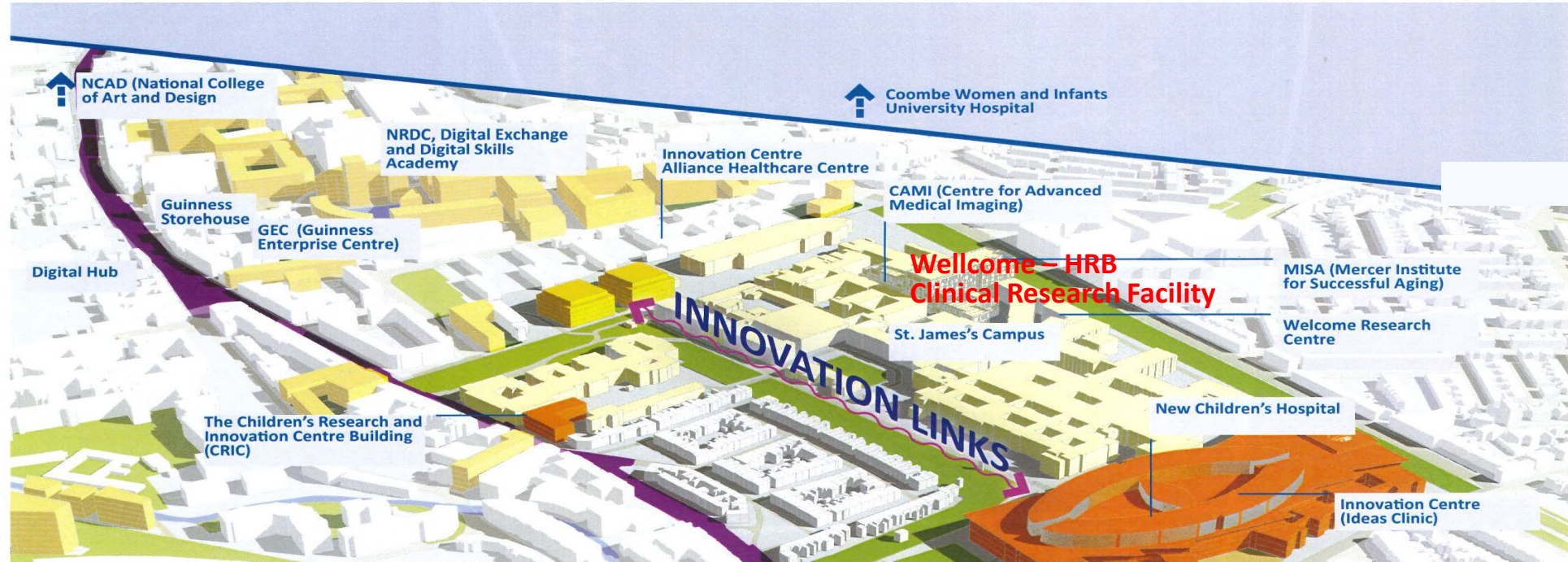
# SJH-Wellcome-HRB CRF Capabilities

<b>Capabilities</b>	Clinical Trial Expertise	Research Pharmacy	Advanced Therapies Capability	Enabling the Academic Trial Ecosystem	Extensive Network
	<ul style="list-style-type: none"> <li>• Study start up</li> <li>• Research nursing</li> <li>• Quality &amp; regulatory Affairs</li> <li>• Pharmacy</li> <li>• Budgeting &amp; contracting</li> </ul>	<ul style="list-style-type: none"> <li>• Experienced research pharmacy service</li> </ul>	<ul style="list-style-type: none"> <li>• Aseptic compounding unit</li> <li>• Advanced therapeutics suite</li> </ul>	<ul style="list-style-type: none"> <li>• Trial methodology expertise</li> <li>• II Trial experience</li> <li>• Medical devices</li> <li>• Sponsorship</li> <li>• Grant writing</li> </ul>	<ul style="list-style-type: none"> <li>• Local</li> <li>• International</li> </ul>
		High Performing Clinical Trial Unit			
<b>Outcomes</b>	Develop & Promote Academic Research				
	Training & Education				
	Patient Access & Engagement				





# SJH-Wellcome-HRB Clinical Research Facility – Capabilities



**CRI-VALVE**  
R-Ventricular probe  
for tricuspid  
incompetence

**PROVERUM**  
Stent for  
symptomatic  
benign prostatic  
hyperplasia

**SELIO**  
Hydrous gel sealant  
for biopsy-induced  
mediastinal  
pneumothorax

**NEUROMOD**  
Bi-modal  
neuromodulation  
for conditions  
including tinnitus





# SJH-Wellcome-HRB Clinical Research Facility – Training

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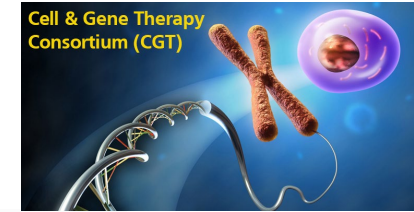
- GCP
- Clinical statistics training
- MD / PhDs students
- Genetics/ genomics
  
- Research Nurse Training Programmes
  
- Research training of postgraduate medical practitioners:
  - Academic Intern / CRF-SHO
  - ICAT



Wellcome / Health Research Board  
**ICAT**  
Irish Clinical Academic Training



# Local & National Relationships





# International Relationships

LE  
RU



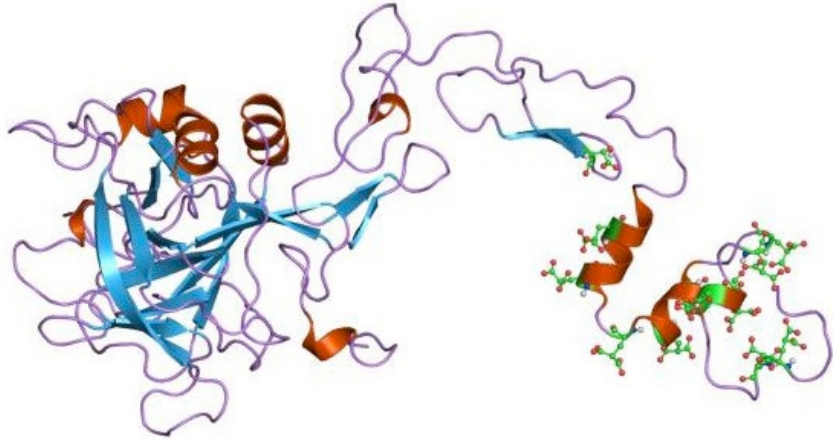
UNIVERSITY OF  
BIRMINGHAM





# Case Study – Haemophilia B Gene Therapy Trial

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- Hemophilia B is an inherited coagulation disorder
  - Hallmark feature is Factor IX deficiency
  - Results in easy bruising and bleeding tendency
- 
- National Centre for Hereditary Coagulation Disorders is based at St James's Hospital
  - Dr Niamh O'Connell, Consultant Hematologist & PI







# Case Study – Haemophilia B Gene Therapy Trial

## HOPE-B Phase 3 Clinical Trial in Haemophilia B

- Phase III, open-label, single-dose, MCT
- Adeno-associated viral vector containing the Padua variant of a codon-optimized human factor IX gene (etranacogene dezaparvovec; AMT-061)
- To demonstrate the non-inferiority of AMT-061 compared to standard routine factor IX prophylaxis (during the lead-in phase) as measured by the annualized bleeding rate (ABR).

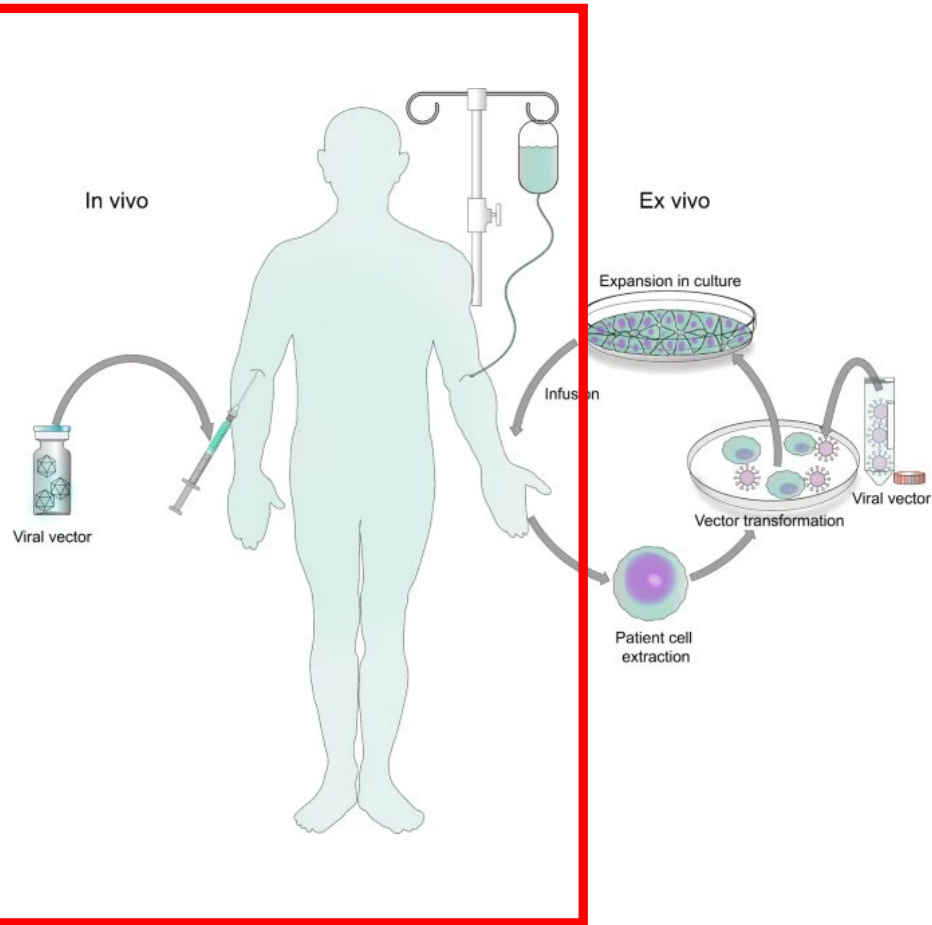


Figure Acknowledgement  
Nature Review 2021



Screening

Lead-in Phase

IMP Dose

Post-treatment Follow-up

Long Term Follow-up





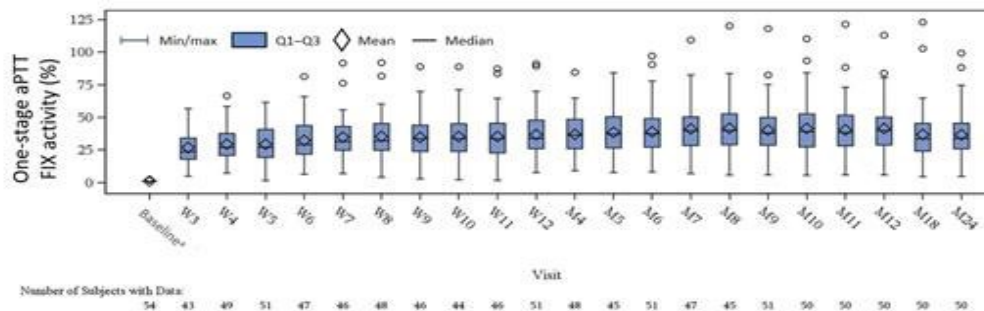
# Case Study – Haemophilia B Gene Therapy Trial

Figure 1. Improvement in ABR: Months 7–24 post-treatment



\*P-value for treated bleeds is not Type I error controlled.  
ABR, annualized bleeding rate; AJBR, annualized joint bleeding rate; ASBR, annualized spontaneous bleeding rate.

Figure 2. FIX activity level over time



Number of Subjects with Data: Baseline: 54; W3: 43; W4: 49; W5: 51; W6: 47; W7: 46; W8: 48; W9: 46; W10: 44; W11: 46; W12: 51; M3: 48; M4: 45; M6: 51; M7: 47; M8: 45; M9: 51; M10: 50; M11: 50; M12: 50; M18: 50; M24: 50.

\* Baseline FIX was imputed based on participant's historical hemophilia B severity documented on the CRF. If the participant had documented severe FIX deficiency (FIX<1%), their baseline FIX activity level was input as 1%. If the participant had documented moderately severe FIX deficiency (FIX≥1% and ≤2%), their baseline FIX activity level was input as 2%. The standard error was not provided at baseline.

aPTT, activated partial thromboplastin time; CRF, case report form; FIX, factor IX; M, Month; W, Week.

- Of 54 participants, 52 (96.%) discontinued and remained free of continuous highly active factor (FIX) prophylaxis from **Day 21 to Month 24**
- Compared with ≥6-month lead-in period mean ABR significantly reduced (64%) during months 7-24 post-treatment
- Sustained FIX activity at Month 6 - 24 post-treatment



# Case Study – Haemophilia B Gene Therapy Trial

Ireland

## Gene therapy used in clinical trial for person with haemophilia

Development hailed as ‘momentous occasion for the haemophilia community in Ireland’

Expand



The Irish Haemophilia Society (IHS) confirmed on Thursday morning that the person received gene therapy as part of a clinical trial. Photograph: iStock

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FDA NEWS RELEASE

## FDA Approves First Gene Therapy to Treat Adults with Hemophilia B

Share Tweet LinkedIn Email Print

For Immediate Release: November 22, 2022

Today, the U.S. Food and Drug Administration approved Hemgenix (etranacogene dezaparvovec), an adeno-associated virus vector-based gene therapy for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

“Gene therapy for hemophilia has been on the horizon for more than two decades. Despite advancements in the treatment of hemophilia, the prevention and treatment of bleeding episodes can adversely impact individuals’ quality of life,” said Peter Marks, M.D., Ph.D., director of the FDA’s Center for Biologics Evaluation and Research. “Today’s approval provides a new treatment option for patients with Hemophilia B and represents important progress in the development of innovative therapies for those experiencing a high burden of disease associated with this form of

Content current as of: 11/22/2022

Regulated Product(s) Biologics

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# Summary & Conclusion

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- CRF at St James's Hospital has significant experience in the conduct of industry sponsored & academic clinical trials
- Experience in the delivery of complex and early phase trials
- Advanced therapy medicinal products (ATMP) capability
- Strong focus on fostering academic research
- Keen interest in collaboration