
BLACKFINBIO
GENE THERAPY – HEALING FROM WITHIN

Background

Sheffield is a major regional gene therapy hub with access to world-class research and infrastructure

Sheffield has a pipeline of preclinical gene therapy products for rare CNS diseases of unmet medical need

GMP AAV manufacturing at the **Sheffield Gene Therapy Innovation and Manufacturing Centre** begins Q3/24

Sheffield's collaborative network is dedicated to feeding through gene therapy and rare disease innovations

Sheffield is leading major international ATMPs initiatives (e.g. www.ardat.org)

Background (2)

BlackfinBio is a University of Sheffield spin-out focused on gene therapy for rare diseases of the CNS

BlackfinBio will leverage Sheffield expertise, infrastructure and AAV platform IP

BlackfinBio is a means to accelerate commercialisation of gene therapy products from University of Sheffield and beyond

Mission

Catalyse and accelerate the clinical development and commercialisation of promising CNS rare disease gene therapy products in order to provide life-changing benefit to patients and address unmet medical needs

Initial Objectives

- Close £2.75m (Founder's) Seed round and incorporate BlackfinBio by Q4 23
- Close £8m Initial Seed round by Q2 25
- Undertake phase I/II trial of SPG47: Start Q7 25
- Evaluate Dopamine deficiency diseases suitable for AAV9 gene therapy
- Identify further pipeline opportunities

Leadership (1)

Peter Nolan | Founder, Chair & CEO – Formerly Director, CBO, and key executive of Oxford Biomedica since its inception; over 25yrs experience in gene therapy commercialization; led negotiations on key deals including Novartis and Sanofi

Chris Edwards | Founder and Chief Business Officer. Father of Robbie who has AP-4 hereditary spastic paraplegia. Seasoned entrepreneur with over 25 yrs experience founding and operating new ventures.

Professor Mimoun Azzouz | Academic Founder, Chief Scientific Officer and Chair of Advisory Board. Chair of Translational Neuroscience at the University of Sheffield; Director of Sheffield GTIMC. Previously Director of Neurobiology at Oxford Biomedica.

Darren Cunningham is Chief Financial Officer of BlackfinBio Ltd. and brings 25 years of experience within the biopharma industry. He is co-founder and former CEO of two biotechs - oncology therapeutics company Inflection Biosciences (Ireland) and autoimmune disease company Mysthera Therapeutics (Switzerland).

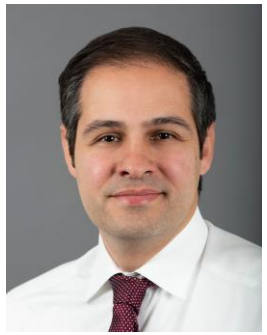
Leadership (2)

Dr Neil Hackett | Regulatory Consultant. Independent consultant based in New York. Extensive experience in pre-clinical development in gene therapy

Advisors

- Goodwin Proctor LLP – Legal
- Symbiotics – Patent Attorneys
- Accenture – IND filing/Clinical
- Boyd Consultants – IND filing/Clinical
- Alacrita LLP – BFB 201 targeting
- Prof Roger Barker – Addenbrookes, Cambridge University
- Prof Manju Kurian – UCL Great Ormond St Hospital

Medical Team



Darius Ebrahimi-Fakhari, MD, PhD
Clinical Lead. Principal investigator, Phase 1/2 Study of BFB-101. Director, Hereditary Spastic Paraplegia Research Program; PI, Spastic Paraplegia Centers of Excellence – Research Network; Director, Movement Disorders Program; Attending Neurologist and Assistant Professor, Boston Children's Hospital & Harvard Medical School.

Professor Manju Kurian, MA MBBChir MRCPCH PhD
Professor of Neurogenetics and an NIHR Research Professor at University College London (UCL)-Great Ormond Street Institute of Child Health, UK. She is also a Consultant Paediatric Neurologist at Great Ormond Street Hospital in London, UK

Professor Stephane Palfi, MD, PhD
Professor of Neurosurgery and Head of the Neurosurgical Department, the Translational Experimental Therapeutics program in Functional Neurosurgery at Henri Mondor Medical Center, Paris University (UPEC). His interests are in developmental therapeutics for Parkinson's disease, Huntington's disease, tremor, dystonia, psychiatric disorders. He has worked extensively in gene therapy for Parkinson's disease, cell grafting for Huntington's and Parkinson's disease as well as primate models of neurodegenerative disorders. He is a principal investigator on numerous preclinical and clinical studies.

Pipeline

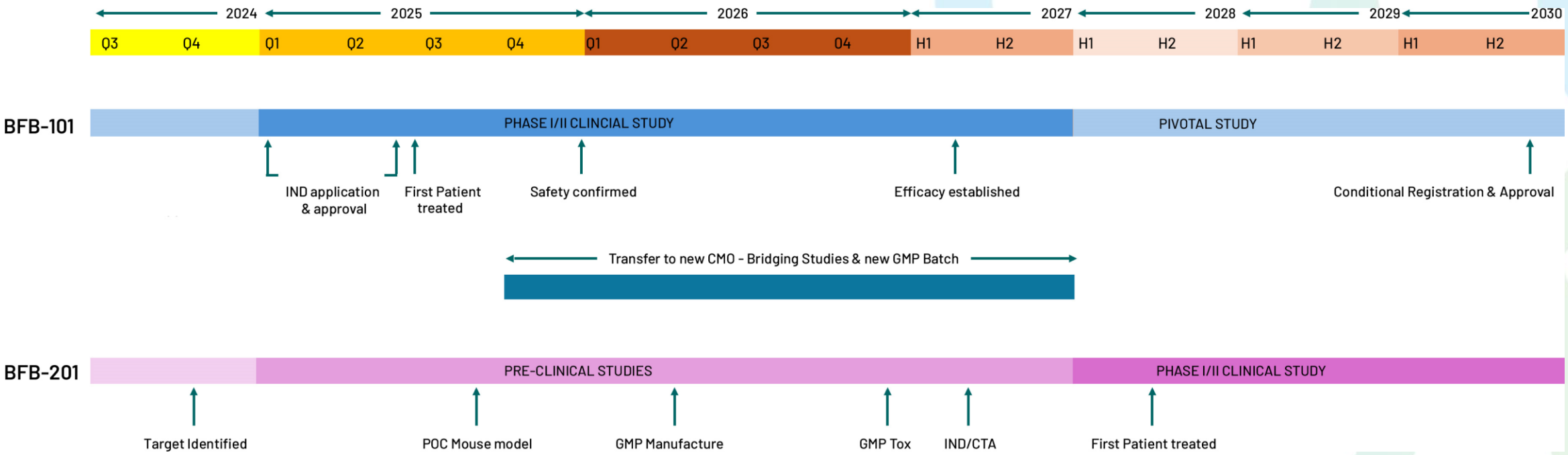
BFB-101

AP4B1 replacement AAV gene therapy for Spastic paraplegia 47 (SPG47), a form of AP-4 Hereditary Spastic Paraplegia (AP-4 HSP)

BFB-201

Dopamine deficiency disease AAV gene therapy using three gene fusion (AADC-TH-CH) – disease targets evaluated and identified for pre-clinical development

Development timeline



BFB-101 | Spastic Paraplegia 47

BFB-101 is gene therapy delivering AP4B1 to treat SPG47

Disease

- SPG47 is a form of AP-4 Hereditary Spastic Paraplegia (AP-4 HSP), an ultra-rare (<5000 patients) progressive neurodevelopmental and neurodegenerative disease with no disease-modifying treatments featuring early-childhood spasticity, microencephaly and seizures.
- Loss-of-function mutations in the AP4B1 gene cause Spastic Paraplegia 47 (SPG47). Mutations in the three other AP4 genes (AP4M1, AP4E1 and AP4S1) also cause forms of AP-4 HSP (SPG50, -51 and -52).
- AP4 facilitates intracellular trafficking from the trans-Golgi network to the endosomal compartment. Loss of any one AP-4 protein subunit leads to loss of AP-4 function.

BFB-101 | Spastic Paraplegia 47

BFB-101 is gene therapy delivering AP4B1 to treat SPG47

Technology

BFB-101 is a patent-protected AAV9 vector[1] expressing the AP4B1 gene developed with funding from Cure AP-4 and LifeArc by Professor Mimoun Azzouz at the University of Sheffield

BFB-101 will be delivered via the cisterna magna as a single dose for the lifetime of the patient

BFB-101 restores AP4 function in vitro and safely improves motor function in AP4B1 mutant mice

[1] Patents Licensed exclusively (i) WO 2021/2205028 (ii) PCT2023EPO78427

BFB-101 | Current Status

Project	Primary Responsibility	Status
Proof of concept	University of Sheffield, UK	Accepted by FDA in Pre-IND
GLP toxicology - NHP	ERBC, Paris France	In vivo completed with no adverse effects Biodistribution analysis completed
Long term safety - mouse	Jackson Labs, ME	Completed December 2022
Manufacturing	UoS – LifeArc & CureAP4 support	Tox material released and used for GLP NHP safety study GMP schedule for completion Q3, 2024
Clinical study	Boston Children's Hospital	Clinical trial design well advanced BFB IND submission Q1 2025

BFB-201 | Dopamine Deficiency Disease

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Monogenetic Disease Landscape

Dopaminergic enzyme deficiencies

- **Sepiapterin reductase**
- GTPCH-1 – CTP cyclohydrolase
- **PTPS 6-pyruvoyl tetrahydropterine synthase**
- **DHPR – Dihydropterine reductase**
- AADC-Aromatic L-amino acid decarboxylase
- **TH-Tyrosine Hydroxylase**

Parkinsonism syndromes

- Lesch-Nyhan's disease
- Rett's syndrome
- Dopa responsive dystonias
- Early onset Parkinson's disease

Alacrita has undertaken an evaluation and has identified **key targets** within this landscape

BFB-201 | Dopamine Deficiency Disease

Alacrita Report Key Targets

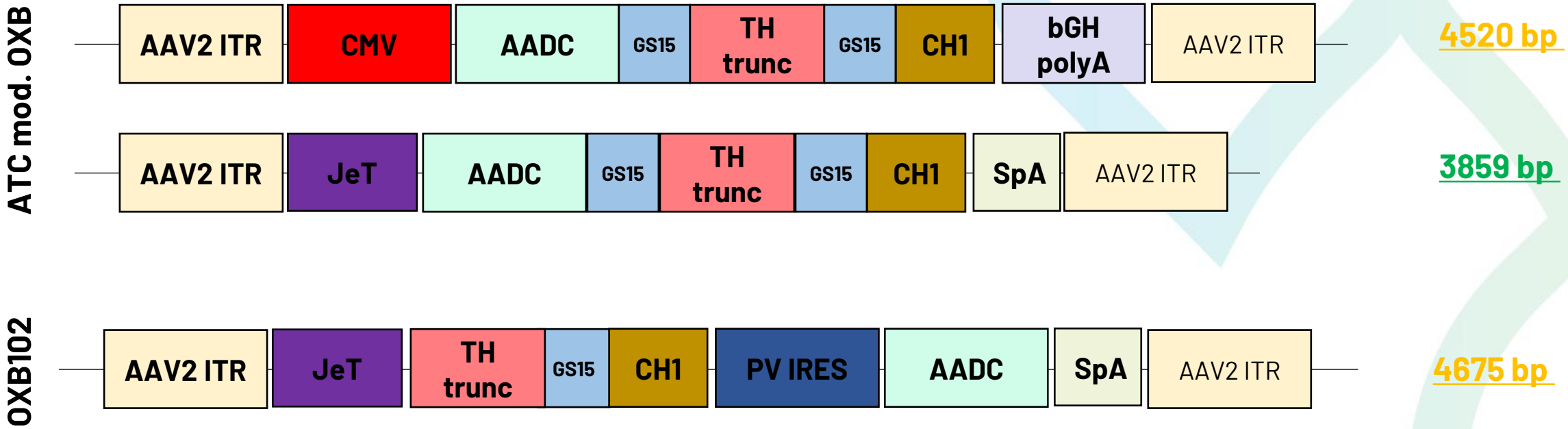
- Sepiapterin reductase
- PTPS 6-pyruvoyl tetrahydropterine synthase
- DHPR – Dihydropterine reductase
- TH-Tyrosine Hydroxylase

These conditions are clinically similar.

Could be treated as a single disorder group using a Master protocol

BFB-201 | Dopamine Deficiency Disease

AAV Vector Design



BFB-201 | Patent Schedule

Country	Patent Application No.	Patent Number	Expiry
WO 2013/ 061076- Construct (OBM 136)			
AU	2012328166	2012328166	26 Oct 2032
CA	2849241	2849241	26 Oct 2032
CA DIV 1	3052407	3052407	26 Oct 2032
CN	201280064927.0	ZL201280064927.0	26 Oct 2032
CN DIV 1	201710722658.7	ZL201710722658.7	
DE	12778779.4	2771471	26 Oct 2032
DE DIV 1	17161437.3	3219801	26 Oct 2032
DK	12778779.4	2771471	26 Oct 2032
EP	12778779.4	2771471	26 Oct 2032
EP DIV 1	17161437.3	3219801	26 Oct 2032
ES	12778779.4	2771471	26 Oct 2032
ES DIV 1	17161437.3	3219801	26 Oct 2032
FR	12778779.4	2771471	26 Oct 2032
FR DIV 1	17161437.3	3219801	26 Oct 2032
GB	12778779.4	2771471	26 Oct 2032
GB DIV 1	17161437.3	3219801	26 Oct 2032
IN	2500/DELNP/2014	378745	26 Oct 2032
IN DIV 1	201918028103	PENDING	26 Oct 2032
IT	12778779.4	2771471	26 Oct 2032
IT DIV 1	17161437.3	3219801	26 Oct 2032
JP	2014-537726	6296987	26 Oct 2032
JP DIV 1	2018-027852	6698114	26 Oct 2032
US	13/661618	10400252	26 Oct 2032
US DIV 1	16/454024	11279954	26 Oct 2032

Repurposing the 3 gene cassette into AAV9 will generate new IP - to be filed in 2025

Competitive Advantage

Pipeline | Market

BlackfinBio will launch with BFB-101, a late preclinical-stage product that has been granted FDA Orphan Drug and Rare Pediatric Disease designations to treat a genetically defined inherited disease

BlackfinBio has undertaken an evaluation of AAV gene therapy for dopamine deficiency diseases and identified target conditions for development

BlackfinBio will identify additional pipeline opportunities

Technology | Intellectual Property

BlackfinBio will leverage both product-specific and platform IP, in addition to extensive know-how and decades of experience in the field, to intelligently, efficiently, and collaboratively advance its pipeline

Approach | Rare Diseases

BlackfinBio will work closely with charities, clinical experts and patient advocacy groups to:

- Accelerate the early stages of product development via a grant-funded, consortium-led approach
- Improve diagnosis rates
- Efficiently find willing patients for clinical trials

Capital requirements (1)

FOUNDERS' SEED STAGE
(Q4 2023) £2.75m

SEED STAGE
(Q3/4 2024) £8m

Use of Capital 2024-27

Establish BFB and senior management team ✅

In-licence BFB-101 ✅

Conclude preclinical studies on BFB-101 ✅

GMP manufacture of BFB-101 vector [Life Arc grant-funded] ✅

Secure IND and commence BFB-101 phase I/II study

BFB-201 Evaluate Dopamine deficiency diseases, secure licence to IP and commence pre-clinical development of chosen target ✅

Identify potential additional pipeline opportunities

Capital requirements (2)

Use of Capital 2027-30

- Plan and undertake PIVOTAL study of BFB-101
- Prepare for Registration by Q4 2030

- File and undertake Phase I/II clinical trial for BFB-201
- Identify and commence development of additional pipeline opportunity

- **SERIES A INVESTMENT: £25-30M**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