

Press release

Northern Gritstone and Argobio Studio back Sheffield University spin-out Crucible Therapeutics

Crucible Therapeutics develops novel therapies treating neurological diseases with significant unmet medical needs, Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal dementia (FTD)

Paris, France, Manchester and Sheffield, United-Kingdom, September 21st, 2023 - Crucible Therapeutics, a biotechnology company developing novel therapies to treat amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease), the most common genetic form of motor neurone disease (MND), and frontotemporal dementia (FTD), has secured £5 million financing from Northern Gritstone and Argobio Studio.

Crucible was founded in the University of Sheffield's internationally renowned Department of Neuroscience by Professor Dame Pamela Shaw, Professor of Neurology and Director of the Sheffield Institute for Translational Neuroscience (SITraN), Professor Guillaume Hautbergue, Professor of Translational RNA Biology, and Professor Mimoun Azzouz, Chair of Translational Neuroscience, SITraN at the University of Sheffield. Research performed by the three scientific founders identified critical factors that contribute to neurotoxicity and neuronal loss in ALS and FTD. They further demonstrated, with support from LifeArc and the Motor Neurone Disease Association, and translational development support from the Cell and Gene Therapy Catapult, that one of these critical factors, SRSF1, could be targeted to improve outcomes in models of ALS and FTD. Crucible will build on its pioneering research by conducting pivotal safety and efficacy studies before proceeding with human clinical trials.

Crucible is receiving financing and support from Northern Gritstone and Argobio Studio to fund essential development and manufacturing work, which will take the company up to its first clinical trial. It is the first spinout focusing on advanced therapeutics to receive investment from Northern Gritstone, the investment business focused on university spin-outs and technology-enabled businesses in the North of England. Argobio Studio is a pan-European biotech company start-up vehicle whose experienced team of entrepreneurs and scientific directors has supported multiple advanced therapeutics start-ups across Europe since inception. Demonstrating its ongoing commitment, Argobio Studio continues to offer operational guidance to Crucible throughout its spinout phase and will persist in providing support during the upcoming preclinical development stage.

Neill Moray Mackenzie and Jonathan Foley from Argobio Studio will support the development of the company's novel therapies. Together their considerable R&D, commercial and manufacturing experience in multiple gene therapy companies will be brought to bear at this critical time for Crucible. Professor Guillaume Hautbergue will join them as Non-Executive Director on the board of Crucible Therapeutics representing the founders.

Professor Dame Pamela Shaw, Co-Founder of Crucible Therapeutics, Professor of Neurology at the University of Sheffield and Director of the Sheffield Institute for Translational Neuroscience (SITraN), said: *"Our novel therapeutic approach has made significant strides in our pursuit of transforming how these devastating diseases are treated and with the potential to achieve meaningful*

therapeutic impact. Today marks an important milestone, which brings us closer to supplying transformative treatments to people with neurological diseases like ALS (also known as motor neuron disease) and FTD. The significant experience and support that Northern Gritstone and Argobio Studio bring to Crucible further enables our pre-clinical development, and in parallel, allows us to strategically build our translational team."

Duncan Johnson, CEO of Northern Gritstone, said: *"Crucible's founders, Pamela, Guillaume and Mimoun, exemplify the world-leading scientific and medical expertise that exists in the North of England. We are delighted to be backing Crucible and we look forward to working with them as they prepare to bring the company's therapeutic candidate closer to clinical trials. We also welcome the opportunity to invest alongside the team at Argobio Studio whose invaluable experience in gene therapy will be critical as Crucible takes the first important step in its journey."*

Neill Moray Mackenzie, Entrepreneur in Residence, Partner at Argobio Studio, said: *"Ever since I had tea with Stephen Hawking in Cambridge many years ago, I have been searching for a realistic hope of a cure for this devastating disease out of respect for him. At Argobio Studio, we have the opportunity to look at all the technologies with unbiased view and I can honestly say the Sheffield approach was the most compelling for us. While the therapy is still in early stages of development, we look forward to working alongside Northern Gritstone to bring the programme to fruition."*

Notes to Editors

About ALS (also known as MND)

ALS (also known as MND) is a neurodegenerative disease which causes nerve cells which control muscle function to progressively stop working throughout the spinal cord and the brain. The disease, which predominantly affects people aged 60-65, leads to progressive paralysis and death usually within three to six years from the onset of symptoms. FTD involves the degeneration of frontal and temporal lobes of the brain causing altered personality features. It most commonly affects people aged 45-65 and can affect behaviour, personality, language and movement. There is currently no effective treatment for ALS or for FTD.

About the Founders

Professor Dame Pamela Shaw is an internationally renowned clinician and academic researcher known for her work in the field of ALS/MND. Pamela is a Consultant Neurologist at the Sheffield Teaching Hospitals NHS Foundation Trust and Professor of Neurology and Director of the Sheffield Institute of Translational Neuroscience (SITraN), where the academic research underpinning Crucible's therapeutic candidate was developed. The range of Pamela's molecular, genetic and clinical contributions has attracted international recognition and the award of multiple prizes, including a Wellcome Trust Senior Fellowship in Clinical Science and an NIHR Senior Investigator award. In 2014, she was made a Dame Commander of the Order of the British Empire (DBE) and, in 2022 she received the British Neuroscience Association award for an outstanding contribution to neuroscience. Her translational research had led to several improved outcomes for patients with MND.

Professor Mimoun Azzouz is a highly accomplished researcher and expert in the field of gene therapy. With an extensive background in neuroscience and molecular biology, he has made significant contributions to the development of innovative gene-based treatments for neurological disorders. His research focuses on the delivery of therapeutic genes to the central nervous system, particularly in

the context of neurodegenerative diseases like Parkinson's, MND and spinal muscular atrophy. Driven by a passion for translational science, Mimoun Azzouz's work bridges the gap between bench and bedside, aiming to bring promising therapies from the laboratory to clinical application. Through his pioneering efforts, he has emerged as a leading figure in the field of gene therapy for neurological conditions, offering hope for patients worldwide.

Professor Guillaume Hautbergue is a distinguished researcher renowned for his contributions in the field of ribonucleic acid (RNA) biology and molecular neuroscience. With an impressive academic background, he has made significant strides in understanding the molecular mechanisms underlying neurodegenerative diseases. His expertise lies in investigating RNA metabolism and its implications in conditions such as motor neuron disease (MND). Professor Hautbergue's groundbreaking research has garnered international recognition, and his findings hold promise for the development of novel therapeutic strategies. Through his unwavering dedication to advancing neuroscience knowledge, Professor Hautbergue continues to shape the field and inspire future generations of researchers. In 2019, he was invited and elected Fellow of the Royal Society of Biology (FRSB) in recognition of “a prominent contribution to the advancement of the Biological Sciences.”

Neill Moray Mackenzie is a seasoned veteran in the biotech industry, boasting a wealth of experience and expertise. With a career spanning several decades, he has played a pivotal role in shaping and advancing the field of biotechnology. Throughout his professional journey, Mackenzie has held key leadership positions in prominent biotech companies, overseeing strategic initiatives, business development, and successful commercialization of innovative therapies. His keen business acumen, combined with his in-depth understanding of scientific advancements, has contributed to his reputation as a visionary leader in the biotech sector. Neill Moray Mackenzie continues to drive growth and innovation, propelling the industry forward with his remarkable contributions.

Jonathan Foley is Scientific Director at Argobio with 20 years of experience in drug discovery, analytical development, and rare disease research. Most recently, Jonathan was a Senior Director and Head of Discovery at Freeline (Nasdaq: FRLN). Prior to Freeline, he was a Lecturer at University College London in the group of gene therapy pioneer Professor Amit Nathwani and was a member of the first research team that spun Freeline out of academia. During his academic career he published extensively in the areas of biochemistry, bleeding disorders and complement-mediated disease.

About Crucible Therapeutics

In 2023, Crucible emerged as a spin-out from the University of Sheffield, focusing on the development of groundbreaking therapies aimed at addressing the significant unmet medical needs in neurological diseases. The foundation of Crucible is built upon the groundbreaking research conducted by world-renowned scientists at SITraN (Sheffield Institute for Translational Neuroscience). As a pre-clinical stage biotech company, Crucible is diligently advancing therapeutic candidates specifically designed to tackle conditions such as Amyotrophic Lateral Sclerosis (ALS), also known as classic MND and Frontotemporal Dementia (FTD). Through their innovative approach, Crucible aims to revolutionize the treatment landscape and bring hope to those affected by these debilitating conditions.

About Argobio Studio

Argobio is a start-up studio based in Paris, France, dedicated to turning cutting-edge innovations into breakthrough biotech companies. Argobio sources innovative early-stage projects on therapeutics from renowned European academic research institutions with a focus on rare diseases, neurological disorders, oncology, and immunology.

Argobio selects and incubates these projects with the goal to create biotech companies and develop them up to a significant Series A financing. Argobio provides broad expertise in the discovery and development of novel drugs with a team of highly experienced Biotech entrepreneurs.

For more information please go to: www.argobiostudio.com Follow us on [LinkedIn](#).

About Northern Gritstone

Northern Gritstone is a groundbreaking investment company, which is dedicated to supporting the commercialisation of academic spin-outs and IP-rich businesses based in the North of England.

Launched in July 2021 by the Universities of Leeds, Manchester and Sheffield, it was founded with the philosophy of Profit with Purpose, combining strong returns for investors with wider positive, societal and economic impact, including supporting Levelling Up and high-skilled job creation in the North of England.

The company is deploying more than £300m of capital, having secured commitments from a broad and diverse base of investors including British Patient Capital, Greater Manchester Pension Fund, West Yorkshire Pension Fund, M&G and Columbia Threadneedle, among others. It is dedicated to financing companies in some of the UK's fastest growing sectors such as advanced materials, energy, health technology and cognitive computation and has already made 11 investments in some of the UK's most exciting future science and technology-enabled businesses.

For more information, please go to: <https://northern-gritstone.com>

About the Founding Universities

The Universities of Leeds, Manchester and Sheffield are renowned education and research institutions that have built a strong reputation for innovation across multiple sectors for nearly 200 years. Each University is a trusted long-term strategic partner to many of the world's best-known businesses across multiple industry sectors.

Combined, the Universities share a talent pool of over 8,400 dedicated researchers, 11,000 academic staff, and 33,000 postgraduate students and generate an annual income of over £2.6 billion. They have been the home to 38 Nobel prize winners and continue to host some of the UK's leading research institutes developing new insights and solutions into business development and sustainable growth.

In total the Founding Universities produce 1 in 11 of all patents and 1 in 5 of every IP licence filed by Higher Education institutes in the UK and are number 1 ranked by research income.

About Cell and Gene Therapy Catapult

The Cell and Gene Therapy Catapult is an independent innovation and technology organisation committed to the advancement of cell and gene therapies with a vision of a thriving industry delivering life changing advanced therapies to the world. Its aim is to create powerful collaborations which overcome challenges to the advancement of the sector. With over 400 experts covering all aspects of advanced therapies, it applies its unique capabilities and assets, collaborates with academia, industry and healthcare providers to develop new technology and innovation.

About LifeArc

LifeArc is a self-funded, not-for-profit medical research organisation. We take science ideas out of the lab and help turn them into medical breakthroughs that can be life-changing for patients. We have been doing this for more than 25 years and our work has resulted in five licensed medicines, including cancer drug pembrolizumab (Keytruda®), lecanemab for Alzheimer's (Leqembi), and a diagnostic for antibiotic resistance.

Our teams are experts in drug and diagnostics discovery, technology transfer, and intellectual property. Our work is in translational science – bridging the gap between academic research and clinical development, providing funding, research and expert knowledge, all with a clear and unwavering commitment to having a positive impact on patient lives. LifeArc is committed to spending £1.3 billion by 2030 in areas of high unmet medical need. LifeArc is a company limited by guarantee (registered in England and Wales under no. 2698321) and a charity (registered in England and Wales under no. 1015243 and in Scotland under no. SC037861).

Find out more about our work on www.lifearc.org or follow us on [LinkedIn](#) or [Twitter](#).

Contacts:

Headland (PR adviser to Northern Gritstone)

Viktor Tsvetanov, northerngritstone@headlandconsultancy.com, 078 8466 7775

NewCap (PR adviser to Argobio Studio)

Arthur Rouillé, arouille@newcap.fr, +33 (0)1 44 71 00 15