RNS Number : 8574V
Syncona Limited
04 February 2025

4 February 2025

Syncona Limited

Spur announced positive data from Phase I/II trial of FLT201 in Gaucher disease

Syncona Ltd, ("Syncona"), a leading life science investor focused on creating, building and scaling a portfolio of global leaders in life science, today notes that its portfolio company, Spur Therapeutics ("Spur") announced positive new data from its Phase I/II GALILEO-1 study of FLT201, its novel gene therapy candidate, in Gaucher disease at the 21st Annual WORLD*Symposium* in San Diego, CA, USA.

Six patients have been treated in GALILEO-1 with a single infusion of FLT201 at a low dose of 4.5e11 vg/kg and have been followed for between nine and 17 months after dosing. All six patients are included in the safety analysis; one patient with detectable pre-existing neutralising antibodies to the AAVS3 capsid was excluded from the efficacy analysis. Prior to the trial all of the patients had been treated with existing therapies enzyme replacement therapy (ERT) or substrate reduction therapy (SRT).

These data follow yesterday's announcement that Spur had received positive feedback from its end-of-Phase II meeting with the US Food and Drug Administration (FDA), with alignment on the potential to seek accelerated approval[1] based on reductions in glucosylsphingosine (lyso-Gb1), an established biomarker of clinical response in Gaucher disease. Full approval would be based on a primary endpoint of maintenance or improvement in haemoglobin at one year in the Phase III study. The completion of the pivotal stage of the Phase III trial in CY2027 is a key value inflection point for Syncona[2].

Data as of 6 December 2024 demonstrated:

- Continued favourable safety and tolerability profile, with no infusion reactions, dose limiting toxicities or treatment-related severe adverse events
- Durable reductions in lyso-Gb1, ranging from 33% to 96% in patients who entered the trial with high levels
    - Stable lyso-Gb1 levels for more than a year after the withdrawal of prior therapy in the one patient who entered the trial with well-controlled levels.
- Maintenance of normal haemoglobin levels (Phase III primary endpoint) beyond a year after withdrawal of ERT or SRT
- Sustained improvements or maintenance in platelet counts and spleen and liver volume after withdrawal of ERT or SRT
- Improvements in bone marrow burden (BMB) in four of the five patients, indicating the clearance of substrate and reappearance of healthy marrow, and maintenance of BMB in the fifth patient. Previously reported BMB scores have been updated to correct a reporting error by an outside clinical research organisation[3]

Chris Hollowood, Chief Executive Officer of Syncona Investment Management Limited and Chair of Spur Therapeutics, said: "These data further reinforce our belief that FLT201 has the potential to be a first- and best-in-class gene therapy for Gaucher disease. Through a single infusion, FLT201 has shown improvements to symptoms that had been persistent in patients receiving approved therapies for years and in some cases decades. We look forward to the initiation of Spur's Phase III FLT201 trial later this year, following the company's recent successful end-of-Phase II meeting with the US FDA."

Spur's announcement is copied below and can be accessed on the company's website at https://spurtherapeutics.com/.

[ENDS]

Enquiries

Syncona Ltd

Natalie Garland-Collins / Fergus Witt
Tel: +44 (0)20 3981 7912

FTI Consulting

Ben Atwell / Tim Stamper
Tel: +44 (0) 20 3727 1000

About Syncona

Syncona's purpose is to invest to extend and enhance human life. We do this by creating, building and scaling companies to deliver transformational treatments to patients in areas of high unmet need.

We aim to build and maintain a diversified portfolio of 20-25 globally leading life science businesses, across development stage, modality and therapeutic area, for the benefit of all our stakeholders. We focus on developing treatments that deliver patient impact by working in close partnership with world-class academic founders and experienced management teams. Our balance sheet underpins our strategy, enabling us to take a long-term view as we look to improve the lives of patients with no or poor treatment options, build sustainable life science companies and deliver strong risk-adjusted returns to shareholders.

ForwardLooking statements - this announcement contains certain forwardlooking statements with respect to the

Forward-looking statements - this announcement contains certain forward-looking statements with respect to the portfolio of investments of Syncona Limited. These statements and forecasts involve risk and uncertainty because they relate to events and depend upon circumstances that may or may not occur in the future. There are a number of factors that could cause actual results or developments to differ materially from those expressed or implied by these forward-looking statements. In particular, many companies in the Syncona Limited portfolio are conducting scientific research and clinical trials where the outcome is inherently uncertain and there is significant risk of negative results or adverse events arising. In addition, many companies in the Syncona Limited portfolio have yet to commercialise a product and their ability to do so may be affected by operational, commercial and other risks.

Syncona Limited seeks to achieve returns over the long term. Investors should seek to ensure they understand the risks and opportunities of an investment in Syncona Limited, including the information in our published documentation, before investing.

Notes

About Key Value Inflection Points

A key value inflection point is a material de-risking event for a portfolio company that has the potential to drive significant NAV growth for Syncona, for example by increasing the possibility of a realisation event, such as M&A. These milestones can also enable companies to access significant capital including through financings and IPOs, which may take place at valuation uplifts and underpin progression to a subsequent key value inflection point which has the potential to drive greater value. M&A or capital access is unlikely to occur immediately following a key value inflection point.

Spur Therapeutics Announces Positive Data from Phase 1/2 GALILEO-1 Trial of FLT201, Its Gene Therapy Candidate for Gaucher Disease, at WORLD*Symposium*™

Oral and poster presentations highlight FLT201's potential to set a new standard of care

LONDON, February 4, 2025 - Spur Therapeutics today announced data from its Phase 1/2 GALILEO-1 trial of FLT201, an adeno-associated virus (AAV) gene therapy candidate for Gaucher disease type 1, showing rapid and sustained improvements in glucosylsphingosine (lyso-Gb1), one of the best predictors of clinical response in Gaucher disease, as well as improvement or maintenance of blood counts, organ volume and bone marrow burden in patients treated with a single infusion of FLT201. FLT201 continues to demonstrate a favorable safety and tolerability profile in all patients treated in the study. These data are being showcased this week in oral and poster presentations at the 21st Annual WORLD*Symposium*.

"Gaucher disease is a debilitating chronic disorder, and despite treatment with currently approved therapies, many patients continue to have serious symptoms," said Pamela Foulds, M.D., Spur's Chief Medical Officer. "Data from our Phase 1/2 study being presented at the WORLD*Symposium* show that a single infusion of FLT201 led to improvements in persistent symptoms and disease involvement in patients who have been on approved therapies for years. These improvements, together with the favorable safety profile and durability of responses, highlight FLT201's potential to provide better efficacy and dramatically reduce the treatment burden for people with Gaucher disease."

"FLT201 is the result of our unwavering focus on developing gene therapies that change people's lives," said Michael Parini, Spur's Chief Executive Officer. "We purposefully designed FLT201 to overcome the shortcomings of currently approved therapies, engineering a more stable version of the GCase enzyme deficient in people with Gaucher disease and packaging it in a capsid that is highly efficient at transducing cells to produce the enzyme. We are seeing that work translate into benefits beyond what current therapies provide at a low dose that we believe could offer an important safety advantage over other gene therapies in development. We are moving quickly to initiate a Phase 3 study of FLT201."

Compelling Safety and Efficacy Data for FLT201

Building on previously reported data, the oral and poster presentations at the WORLD*Symposium* demonstrate the durable benefits and longer-term safety profile of FLT201. In addition to updated safety and tolerability data, the presentations include recent assessments of biomarker and efficacy endpoints from the GALILEO-1 study, a first-in-human, international, multicenter dose-finding study in adults with Gaucher disease type 1, and the GALILEO-2 long-term follow up study.

Six patients were treated in GALILEO-1 with a single infusion of FLT201 at a low dose of 4.5e11 vg/kg. Patients have been followed for between nine and 17 months after dosing and have all rolled over into GALILEO-2. All six patients are included in the safety analysis; one patient with detectable pre-existing neutralizing antibodies to the AAVS3 capsid was excluded from the efficacy analysis. Prior to the trial, patients had been on a stable dose of either enzyme replacement therapy (ERT) or substrate reduction therapy (SRT) for between four and 24 years. All patients taken off ERT or SRT remain off those therapies.

The data as of December 6, 2024 cut-off date demonstrated:

- Favorable safety and tolerability, with no infusion reactions or dose limiting toxicities. All treatment-related adverse events were mild to moderate in nature.
- Durable reductions in lyso-Gb1, ranging from 33% to 96%, in patients who entered the trial with high levels; stable lyso-Gb1 levels for more than a year after the withdrawal of prior therapy in the one patient who entered the trial with well-controlled levels. Lyso-Gb1 levels in the blood are highly correlated with substrate levels in disease-affected tissues as well as with treatment response.
- Maintenance of normal hemoglobin levels beyond a year after withdrawal of ERT or SRT.
- Sustained improvements or maintenance in platelet counts and spleen and liver volume after withdrawal ERT or SRT.
- Improvements in bone marrow burden (BMB) in four of the five patients, indicating the clearance of substrate and reappearance of healthy marrow, and maintenance of BMB in the fifth patient. Previously reported BMB scores have been updated to correct a reporting error by an outside clinical research organization.[4]

As announced yesterday, Spur has gained alignment with the U.S. Food and Drug Administration on the design of a single-arm Phase 3 study to support potential accelerated approval of FLT201 based on reductions in lyso-Gb1 and full approval based on improvement or maintenance of hemoglobin levels. Secondary endpoints will include platelet counts and organ

based on improvement or maintenance of hemoglobin levels. Secondary endpoints will include platelet counts and organ volume, with exploratory endpoints including bone health assessments and patient-reported outcomes. Spur expects to dose the first patient in the Phase 3 study in the second half of 2025.

About FLT201

FLT201 is an adeno-associated virus (AAV) gene therapy candidate in clinical development as a potential one-time treatment for Gaucher disease. FLT201 leverages Spur's proprietary and potent AAVS3 capsid to deliver GCase85, a rationally engineered longer-acting version of the enzyme deficient in people with Gaucher disease, with the goal of stopping disease progression, reducing or eliminating symptoms, and allowing patients to come off current lifelong treatments. Data from the completed Phase 1/2 GALILEO-1 clinical trial of FLT201 have shown improvements across a number of key biomarkers and clinical assessments, including substantial reductions in the toxic buildup of substrate that results from the enzyme deficiency, as well as a favorable safety and efficacy profile. A Phase 3 trial for FLT201 is expected to start in the second half of 2025.

About Gaucher Disease

Gaucher disease is caused by a mutation in the GBA1 gene that results in abnormally low levels of glucocerebrosidase (GCase), an enzyme needed to metabolize a certain type of lipid. As a result, harmful substrates glucosylceramide (Gb-1) and glucosylsphingosine (lyso-Gb1) build up in cells, which then accumulate in tissues and organs throughout the body, causing inflammation and dysfunction. Despite treatment with currently approved therapies, many people with Gaucher disease continue to experience debilitating symptoms, including enlarged organs, fatigue, bone pain and reduced lung function. Gaucher disease affects approximately 18,000 people in the United States, United Kingdom, France, Germany, Spain, Italy and Israel.

About Spur Therapeutics

Spur Therapeutics is a clinical-stage biotechnology company focused on developing life-changing gene therapies for debilitating chronic conditions. By optimizing every component of its product candidates, Spur aims to unlock the true potential of gene therapy to realize outsized clinical results.

Spur is advancing a breakthrough gene therapy candidate for Gaucher disease and a potential first-in-class gene therapy candidate for adrenomyeloneuropathy, as well as a research strategy to move gene therapy into more prevalent diseases, including forms of Parkinson's, dementia, and cardiovascular disease. Expanding our impact, and advancing the practice of genetic medicine.

Toward life-changing therapies, and brighter futures. Toward More™

For more information, visit www.spurtherapeutics.com or connect with Spur on LinkedIn and X.

Investor Contact
Naomi Aoki

naomi.aoki@spurtherapeutics.com

+1 617 283 4298

Media Contact
Carolyn Noyes

carolyn.noyes@spurtherapeutics.com

+1 617 780 2182

---

[1] The FDA's Accelerated Approval Program allows for earlier approval of drugs that treat serious conditions, and fill an unmet medical need based on a surrogate endpoint. The use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval.

[2] The definition of a key value inflection point can be found in the notes section.

[3] For updated scores for each patient, please refer to the overview deck available on the News & Data section of www.spurtherapeutics.com

[4] For updated scores for each patient, please refer to the overview deck available on the News & Data section of www.spurtherapeutics.com.

END

PFUBZLFBELLFBBQ