



SpringWorks Therapeutics Receives Positive CHMP Opinion for Mirdametinib for the Treatment of Adult and Pediatric Patients with NF1-PN

May 23, 2025

– If approved, mirdametinib is expected to be the first and only therapy in the European Union with marketing authorization for both adults and children with NF1-PN –

– Decision from European Commission expected in the third quarter of 2025 –

STAMFORD, Conn., May 23, 2025 (GLOBE NEWSWIRE) -- SpringWorks Therapeutics, Inc. (Nasdaq: SWTX), a commercial-stage biopharmaceutical company focused on severe rare diseases and cancer, announced today that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending the granting of a conditional marketing authorization for mirdametinib, a MEK inhibitor, for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in pediatric and adult patients with neurofibromatosis type 1 (NF1) aged 2 years and above. The European Commission (EC) will review the CHMP opinion and is expected to make a final decision regarding the approval in the third quarter of 2025. If approved, mirdametinib will be available in 1 and 2 mg capsules and in a 1 mg dispersible tablet, which dissolves easily in water.

"The positive opinion from the CHMP brings us one step closer to delivering our medicine to both children and adults with NF1-PN in Europe, who we believe are in need of new therapeutic advances," said Saqib Islam, Chief Executive Officer of SpringWorks. "Upon approval, we look forward to bringing mirdametinib to appropriate patients in Europe as quickly as possible."

NF1 is a genetic disorder that affects approximately 3 in 10,000 people in the EU, or an estimated 135,000 people.^{1,2} Patients with NF1 have approximately a 30 to 50% lifetime risk of developing plexiform neurofibromas, which are tumors that grow in an infiltrative pattern along the peripheral nerve sheath and that can cause severe disfigurement, pain and functional impairment.^{3,4} Plexiform neurofibromas can transform into malignant peripheral nerve sheath tumors, an aggressive and potentially fatal disease.⁵ Surgical removal can be challenging due to the infiltrative tumor growth pattern of plexiform neurofibromas along nerves, and up to approximately 85% of plexiform neurofibromas are considered not amenable to complete resection.^{6,7,8}

"NF1-PN is a genetic disorder that can be highly morbid and unpredictable. It takes a significant physical and emotional toll on patients and their caregivers, and there have been limited treatment options available," said Ignacio Blanco, MD, PhD, Chairman of the National Reference Center for Adult Patients with Neurofibromatosis at Hospital Universitari Germans Trias i Pujol, Spain. "Surgical removal of plexiform neurofibromas can be challenging and is often not possible, so if approved, mirdametinib could be an important treatment option for children and adult patients in Europe."

The CHMP opinion was based on the Marketing Authorization Application (MAA) for mirdametinib, which was validated by the EMA in August 2024. The MAA centered on the primary results from the Phase 2b ReNeu trial, which enrolled 114 patients with NF1-PN age 2 years or older (58 adults and 56 pediatric patients). The study met the primary endpoint of confirmed objective response rate (ORR), as assessed by blinded independent central review, demonstrating an ORR of 41% (N= 24/58) in adults and 52% in children (N=29/56). The median best percentage change in target PN volume was -41% (range: -90 to 13%) in adults and -42% (range: -91 to 48%) in children. Among those with a confirmed response, 88% percent of adults and 90% of children had a response of at least 12 months duration, and 50% and 48%, respectively, had a response of at least 24 months duration. Both adults and children also experienced early and sustained significant improvements from baseline in pain and quality of life as assessed across multiple patient-reported outcome tools.⁹

Mirdametinib demonstrated a manageable safety and tolerability profile. The most common adverse events (>25%) reported in adults receiving mirdametinib were rash, diarrhea, nausea, musculoskeletal pain, vomiting and fatigue. The most common adverse events (>25%) occurring in children were rash, diarrhea, musculoskeletal pain, abdominal pain, vomiting, headache, paronychia, left ventricular dysfunction and nausea.⁹

Mirdametinib is approved in the U.S. for the treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection.

About the ReNeu Trial

ReNeu ([NCT03962543](#)) is an ongoing, multi-center, open-label, single arm, Phase 2b trial evaluating the efficacy, safety and tolerability of mirdametinib in patients ≥2 years of age with an inoperable NF1-associated PN causing significant morbidity. The study enrolled 114 patients to receive mirdametinib at a dose of 2 mg/m² twice daily (maximum dose of 4 mg twice daily) without regard to food. Mirdametinib was administered orally in a 3-week on, 1-week off dosing schedule as either a capsule or dispersible tablet. The primary endpoint is confirmed objective response rate (ORR) defined as the proportion of patients with a ≥20% reduction in target tumor volume on consecutive scans during the 24-cycle treatment phase, as measured by MRI and assessed by blinded independent central review. Secondary endpoints include safety and tolerability, duration of response, and changes in patient-reported outcomes from baseline to Cycle 13. The treatment phase of the trial is complete, and results were presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. Patients who completed the treatment phase were eligible to continue receiving treatment in the optional long-term follow-up portion of the study, which is ongoing.

About NF1-PN

Neurofibromatosis type 1 (NF1) is a rare genetic disorder that arises from mutations in the NF1 gene, which encodes for neurofibromin, a key suppressor of the MAPK pathway.^{10,11} NF1 is the most common form of neurofibromatosis, with an estimated global birth incidence of approximately 1 in 2,500 individuals.^{3,12} In the EU, NF1 affects approximately 3 in 10,000 people, or an estimated 135,000 people.^{1,2} The clinical course of NF1 is

NF patients have approximately a 30%-50% lifetime risk of developing plexiform neurofibromas, or PN, which are tumors that grow in an infiltrative pattern along the peripheral nerve sheath and that can cause severe disfigurement, pain and functional impairment; in rare cases, NF1-PN may be fatal.^{3,4,5} NF1-PNs are most often diagnosed in the first two decades of life.³ These tumors can be aggressive and are associated with clinically significant morbidities; typically, they grow more rapidly during childhood.^{14,15}

About Mirdametinib

The FDA and the European Commission have granted Orphan Drug designation for mirdametinib for the treatment of NF1.

SpringWorks is a commercial-stage biopharmaceutical company dedicated to improving the lives of patients with severe rare diseases and cancer. We developed and are commercializing the first and only FDA-approved medicine for adults with desmoid tumors and the first and only FDA-approved medicine for both adults and children with neurofibromatosis type 1 associated plexiform neurofibromas (NF1-PN). We are also advancing a diverse portfolio of novel targeted therapy product candidates for patients with both solid tumors and hematological cancers.

Forward-Looking Statements

Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements.

Contacts:

Media@Springworkstx.com

Investors@Springworkstx.com

1. Lee TJ, et al. Incidence and prevalence of neurofibromatosis type 1 and 2: a systematic review and meta-analysis. *Orphanet J Rare Dis.* 2023;18(1):292. doi:10.1186/s13023-023-02911-2.
2. Eurostat. Population and population change statistics. Eurostat Statistics Explained. 2024. Available at: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_and_population_change_statistics. Accessed May 8, 2025.
3. Prada C, Rangwala F, Martin L, et al. Pediatric Plexiform Neurofibromas: Impact on Morbidity and Mortality in

- Neurofibromatosis Type 1. *J Pediatr*. 2012;160(3):461-467. doi:10.1016/j.jpeds.2011.08.051.
4. Miller DT, et al. Health supervision for children with neurofibromatosis Type 1. *Pediatrics*. 2019;143(5):e20190660.
 5. Kamaludin, Siti Nurhazwani, et al. "Plexiform neurofibromatosis with peripheral malignant nerve sheath tumor and scoliosis - more surveillance imaging needed?" *Radiology case reports* vol. 17,7 2388-2393. 6 May. 2022, doi:10.1016/j.radcr.2022.03.111.
 6. Needle M, Cnaan A, Dattilo J, et al. Prognostic signs in the surgical management of plexiform neurofibroma: The Children's Hospital of Philadelphia experience, 1974-1994. *J Pediatr*. 1997;131(5):678-682. doi:10.1016/s0022-3476(97)70092-1.
 7. Ejerskov, C., Farholt, S., Nielsen, F.S.K. et al. Clinical Characteristics and Management of Children and Adults with Neurofibromatosis Type 1 and Plexiform Neurofibromas in Denmark: A Nationwide Study. *Oncol Ther* 11, 97–110 (2023). doi:10.1007/s40487-022-00213-4.
 8. Wolkenstein, P. et al. (2023) 'French cohort of children and adolescents with neurofibromatosis type 1 and symptomatic inoperable plexiform neurofibromas: Cassiopea study', *European Journal of Medical Genetics*, 66(5), p. 104734. doi:10.1016/j.ejmg.2023.104734.
 9. Moertel CL, Fisher MJ, Weiss BD, et al. ReNeu: A pivotal, Phase IIb trial of mirdametinib in adults and children with symptomatic neurofibromatosis type 1-associated plexiform neurofibroma. *J Clin Oncol*. 2024;JCO.24.01034. doi:10.1200/JCO.24.01034.
 10. Yap YS, McPherson JR, Ong CK, et al. The NF1 gene revisited - from bench to bedside. *Oncotarget*. 2014;5(15):5873-5892. doi:10.18632/oncotarget.2194.
 11. Rasmussen S, Friedman J. NF1 Gene and Neurofibromatosis 1. *Am J Epidemiol*. 2000;151(1):33-40. doi:10.1093/oxfordjournals.aje.a010118.
 12. Ferner R. Neurofibromatosis 1 and neurofibromatosis 2: a twenty first century perspective. *The Lancet Neurology*. 2007;6(4):340-351. doi:10.1016/s1474-4422(07)70075-3.
 13. Weiss, Brian D et al. "NF106: A Neurofibromatosis Clinical Trials Consortium Phase II Trial of the MEK Inhibitor Mirdametinib (PD-0325901) in Adolescents and Adults with NF1-Related Plexiform Neurofibromas." *Journal of clinical oncology: official journal of the American Society of Clinical Oncology* vol. 39,7 (2021):797-806. doi:10.1200/JCO.20.02220.
 14. Gross A, Singh G, Akshintala S, et al. Association of plexiform neurofibroma volume changes and development of clinical morbidities in neurofibromatosis 1. *Neuro Oncol*. 2018;20(12):1643-1651. doi:10.1093/neuonc/noy067.
 15. Nguyen R, Dombi E, Widemann B, et al. Growth dynamics of plexiform neurofibromas: a retrospective cohort study of 201 patients with neurofibromatosis 1. *Orphanet J Rare Dis*. 2012;7(1):75. doi:10.1186/1750-1172-7-75.