SpringWorks® THERAPEUTICS

I always wear my hair down to cover the plexiform on my neck. I only wear my hair up if I really, really have to.

– Krista, living with NF1-PN

COPING ISN'T CARE.

Patients with neurofibromatosis type 1 with plexiform neurofibromas (NF1-PN) may use coping mechanisms to normalize the burden of their condition, but the adjustments they make are not an alternative to the care they need.

You have the expertise and skills to help patients manage their NF1-PN.

What is NF1-PN?

- **Neurofibromatosis type 1 (NF1) is an incurable genetic condition** affecting ~1 in 2500 newborns worldwide that is caused by a pathogenic variant in the NF1 tumor suppressor gene[1,2]
- Peripheral nerve sheath tumors called **plexiform neurofibromas (PNs)** are a common clinical manifestation of NF1[1]

30% TO 50%
of children and adults with NF1 develop PNs[1,3,4]

- **Malignant transformation may occur**; malignant peripheral nerve sheath tumors (MPNSTs) occur in up to 16% of patients with NF1 and are associated with a **5-year overall survival rate** of 35% to 50%[5-7]

PNs are highly invasive and often cause debilitating morbidities[4,8]

- Patients often experience **pain**, **disfigurement**, compression of internal organs, **impaired physical function**, and reduced quality of life

In a survey about NF1-PN burden[9,*]:

64.6%
REPORTED PAIN

In a study of patients with NF1-PN[8,†]:

47.7%
EXPERIENCED DISFIGUREMENT
(41/86)

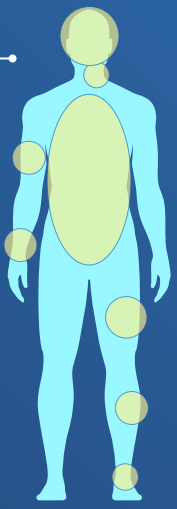
*Based on a cross-sectional study using a one-time survey of NF1-PN patients and caregivers in the United States. Sixty-one pediatric patients 8 to 18 years old and their caregivers, and 21 additional caregivers of patients 2 to 7 years old (total of 82 caregivers) participated in the survey.[9]

†Based on a retrospective analysis of 491 NF1 patients followed at 2 reference centers in Brazil.[8]

SpringWorks® THERAPEUTICS

NF1-PN can be a complex disease to manage

- PNs can grow anywhere on the body outside of the central nervous system; **the most common location is the head and neck area**, followed by the extremities and trunk[3,8,*,†]
- The **growth rate of PNs is unpredictable,** and there may be periods of rapid growth followed by periods of relative inactivity[10–13]

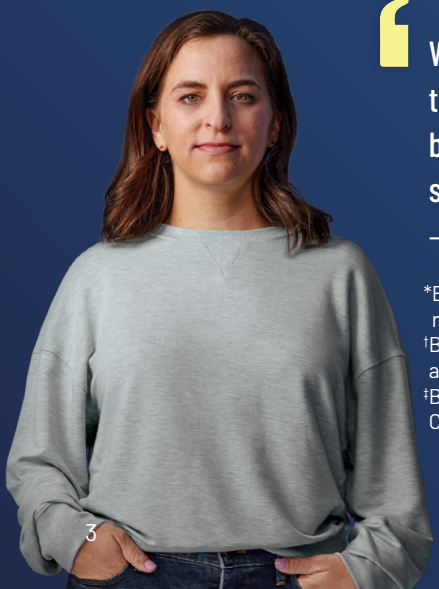


Surgery is not always an option

- **NF1-PN surgery is often restricted** by tumor site or infiltration of surrounding nerves and vasculature[14]
- Even when surgery is feasible, complete removal of a PN is not possible in many cases[3,15]

~50% of patients
have **tumors that cannot be completely resected**[16]

20% of tumors regrow
after a reported **complete resection**[14,‡]



> When I was younger, I wondered what people thought when they saw the PN on my leg because it's visible when I'm wearing a bathing suit and it was kind of embarrassing.
>
> *— Lindsey, living with NF1-PN*

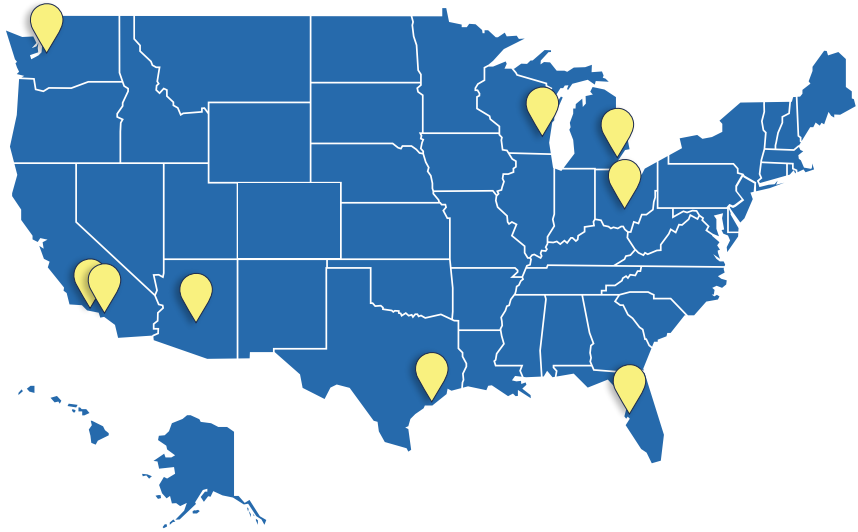
*Based on a retrospective analysis of 491 NF1 patients followed at 2 reference centers in Brazil.[8]
†Based on a retrospective analysis of 154 pediatric NF1-PN patients seen at Cincinnati Children's Hospital Medical Center between 1997 and 2007.[3]
‡Based on a retrospective review of 121 NF1-PN patients seen at the Children's Hospital of Philadelphia between 1974 and 1994.[14]

SpringWorks® THERAPEUTICS

NF1-PN can be especially challenging for adult patients

As children, the logistics of NF1-PN care are likely managed by their caregivers or within a neurofibromatosis (NF) clinic. **However, adult patients have fewer options for where they can receive specialized care.**[17,18]

Adult-only clinics within the NF Clinic Network (US)



Adapted from the Children's Tumor Foundation website. For illustrative purposes only.

Many patients disengage from care during the transition to adulthood

For young adult patients, the added responsibility of managing their own care may feel overwhelming. They frequently drop out of care due to a number of reasons, including[17,19-24,*]:

- Financial and travel barriers
- Difficulty coordinating appointments
- Lack of approved treatment options
- An unwillingness to monitor tumors that aren't causing acute symptoms

*Based on SpringWorks Therapeutics–sponsored market research that included 4 adult NF1-PN patients and 11 NF1-PN caregivers in the United States. Both patients and caregivers were asked to identify the emotional and experiential impact of NF1-PN on patients.[23]

SpringWorks® THERAPEUTICS

Tips for helping patients transition between pediatric and adult care

If you're caring for a patient, talk to them about the importance of keeping up with their NF1-PN care as they enter adulthood. Earlier detection of changes in PNs can lead to earlier management.[10,25]

- Discuss the transition of care early to help patients prepare[26]
- Refer patients to healthcare providers (HCPs) who are within driving distance of where patients live[20,26]
- If there are no local specialists where the patient primarily resides, you may want to work to establish a local HCP (eg, primary care provider) who can monitor them in conjunction with a specialist in another town[20]
- Work with the patient to discuss practical concerns (eg, travel barriers, insurance)[26]
- Work with care coordinators, if possible[27]

> I remember seeing my pediatrician a couple weeks before leaving for college. He checked me out and told me to take care of myself. That was it.
>
> *— Antwan, living with NF1-PN*

SpringWorks® THERAPEUTICS

Patients learn to cope with their symptoms, but this is not an alternative to care

Many patients with NF1-PN choose not to seek care from a medical professional for their symptoms. Some normalize their challenges, adopting coping mechanisms to adjust to the condition.[20,23,24,28]

Some patients return to care only when symptoms like pain become unbearable* or they have an acute concern (eg, family planning). Current guidelines and clinical practice recommendations emphasize the **need for continuous monitoring at regular intervals**.[4,10,17,23,25,28-30]

*Based on SpringWorks Therapeutics–sponsored market research that included 4 adult NF1-PN patients and 11 NF1-PN caregivers in the United States. Both patients and caregivers were asked to identify the emotional and experiential impact of NF1-PN on patients.[23]

SpringWorks® THERAPEUTICS

Considerations to help patients stay engaged in their NF1-PN care

Stressing the importance of monitoring

- Remind patients that monitoring is a vital part of staying on top of their NF1-PN and about why having a local HCP who can monitor them in between specialty appointments is important[10,25,29]
  - **Even if there are no acute symptoms, a PN may be growing or transforming into an MPNST.** Once a PN has transformed into an MPNST, mortality risk greatly increases[5-7]

During an annual physical exam that includes blood and lab work, patients should be assessed for signs and symptoms, including pain, mobility issues, and changes in size, volume, or texture of tumors.[25]

> I'm lucky that my childhood doctor sees adult patients with NF. As an adult, sometimes it's harder to find neurologists or specialists who will see you because you're no longer a pediatric patient.
>
> *– Krista, living with NF1-PN*

SpringWorks® THERAPEUTICS

Visit NF1PN.com to get the latest information and sign up to receive updates.

SpringWorks® THERAPEUTICS

References: 1. Ejerskov C, Farholt S, Nielsen FSK, et al. Clinical characteristics and management of children and adults with neurofibromatosis type 1 and plexiform neurofibromas in Denmark: a nationwide study. *Oncol Ther*. 2023;11(1):97-110. **2.** Lee T-SJ, Chopra M, Kim RH, Parkin PC, Barnett-Tapia C. Incidence and prevalence of neurofibromatosis type 1 and 2: a systematic review and meta-analysis. *Orphanet J Rare Dis*. 2023;18(1):292. **3.** Prada CE, Rangwala FA, Martin LJ, et al. Pediatric plexiform neurofibromas: impact on morbidity and mortality in neurofibromatosis type 1. *J Pediatr*. 2012;160(3):461-467. **4.** Miller DT, Freedenberg D, Schorry E, Ullrich NJ, Viskochil D, Korf BR; Council on Genetics; American College of Medical Genetics and Genomics. Health supervision for children with neurofibromatosis type 1. *Pediatrics*. 2019;143(5):e20190660. **5.** Higham CS, Dombi E, Rogiers A, et al. The characteristics of 76 atypical neurofibromas as precursors to neurofibromatosis 1 associated malignant peripheral nerve sheath tumors. *Neuro Oncol*. 2018;20(6):818-825. **6.** Miettinen MM, Antonescu CR, Fletcher CDM, et al. Histopathologic evaluation of atypical neurofibromatous tumors and their transformation into malignant peripheral nerve sheath tumor in patients with neurofibromatosis 1—a consensus overview. *Hum Pathol*. 2017;67:1-10. **7.** Zehou O, Fabre E, Zelek L, et al. Chemotherapy for the treatment of malignant peripheral nerve sheath tumors in neurofibromatosis 1: a 10-year institutional review. *Orphanet J Rare Dis*. 2013;8:127. **8.** Darrigo LG Jr, Ferraz VEF, Cormedi MCV, et al. Epidemiological profile and clinical characteristics of 491 Brazilian patients with neurofibromatosis type 1. *Brain Behav*. 2022;12(6):e2599. **9.** Yang X, Yoo HK, Amin S, et al. Clinical and humanistic burden among pediatric patients with neurofibromatosis type 1 and plexiform neurofibroma in the USA. *Childs Nerv Syst*. 2022;38(8):1513-1522. **10.** Ferner RE, Huson SM, Thomas N, et al. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. *J Med Genet*. 2007;44(2):81-88. **11.** Akshintala S, Baldwin A, Liewehr DJ, et al. Longitudinal evaluation of peripheral nerve sheath tumors in neurofibromatosis type 1: growth analysis of plexiform neurofibromas and distinct nodular lesions. *Neuro Oncol*. 2020;22(9):1368-1378. **12.** Ly KI, Merker VL, Cai W, et al. Ten-year follow-up of internal neurofibroma growth behavior in adult patients with neurofibromatosis type 1 using whole-body MRI. *Neurology*. 2023;100(7):e661-e670. **13.** Nguyen R, Dombi E, Widemann BC, et al. Growth dynamics of plexiform neurofibromas: a retrospective cohort study of 201 patients with neurofibromatosis 1. *Orphanet J Rare Dis*. 2012:7:75. **14.** Needle MN, 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. **15.** Yang X, Desai K, Agrawal N, et al. Treatment, resource use and costs among pediatric patients with neurofibromatosis type 1 and plexiform neurofibromas. *Pediatric Health Med Ther*. 2020;11:421-428. **16.** *Selumetinib for Treating Symptomatic and Inoperable Plexiform Neurofibromas Associated With Type 1 Neurofibromatosis in Children Aged 3 and Over*. National Institute for Health and Care Excellence; May 5, 2022. HST20. Accessed April 11, 2024. https://www.nice.org.uk/guidance/hst20 **17.** Radtke HB, Berger A, Skelton T, Goetsch Weisman A. Neurofibromatosis type 1 (NF1): addressing the transition from pediatric to adult care. *Pediatric Health Med Ther*. 2023;14:19-32. **18.** Gregory TA, Molina PSB, Phillips GD, Henson JW. Impact of neurofibromatosis type 1 in an adult community population. *Neurooncol Pract*. 2022;9(3):229-235. **19.** Lai J-S, Jensen SE, Patel ZS, Listernick R, Charrow J. Using a qualitative approach to conceptualize concerns of patients with neurofibromatosis type 1 associated plexiform neurofibromas (pNF) across the lifespan. *Am J Med Genet A*. 2017;173(1):79-87. **20.** Rietman AB, van Helden H, Both PH, et al. Worries and needs of adults and parents of adults with neurofibromatosis type 1. *Am J Med Genet A*. 2018;176(5):1150-1160. **21.** Siegel A, Lockridge R, Struemph KL, et al. Perceived transition readiness among adolescents and young adults with neurofibromatosis type 1 and plexiform neurofibromas: a cross-sectional descriptive study. *J Pediatr Psychol*. 2024:jsae006. **22.** Goetsch Weisman A, Haws T, Lee J, Lewis AM, Srdanovic N, Radtke HB. Transition readiness assessment in adolescents and young adults with neurofibromatosis type 1 (NF1). *Compr Child Adolesc Nurs*. 2023;46(3):223-239. **23.** Data on file: SpringWorks Therapeutics, Inc. **24.** Foji S, Mohammadi E, Sanagoo A, Jouybari L. How do people with neurofibromatosis type 1 (the forgotten victims) live? a grounded theory study. *Health Expect*. 2022;25(2):659-666. **25.** Stewart DR, Korf BR, Nathanson KL, Stevenson DA, Yohay K. Care of adults with neurofibromatosis type 1: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2018;20(7):671-682. **26.** The six core elements of health care transition 3.0. Got Transition. Accessed April 11, 2024. https://gottransition.org/6ce/?side-by-side **27.** Sandquist M, Davenport T, Monaco J, Lyon ME. The transition to adulthood for youth living with rare diseases. *Children (Basel)*. 2022;9(5):710. **28.** Oates EC, Payne JM, Foster SL, Clarke NF, North KN. Young Australian adults with NF1 have poor access to health care, high complication rates, and limited disease knowledge. *Am J Med Genet A*. 2013;161A(4):659-666. **29.** Fisher MJ, Blakeley JO, Weiss BD, et al. Management of neurofibromatosis type 1-associated plexiform neurofibromas. *Neuro Oncol*. 2022;24(11):1827-1844. **30.** Armstrong AE, Belzberg AJ, Crawford JR, Hirbe AC, Wang ZJ. Treatment decisions and the use of MEK inhibitors for children with neurofibromatosis type 1-related plexiform neurofibromas. *BMC Cancer*. 2023;23(1):553.

SpringWorks® THERAPEUTICS