CTF and NF1-PEARL

Advancing treatments for unmet needs in NF1

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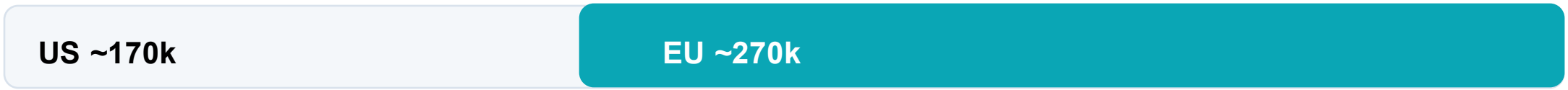
TEDDY Scientific Meeting, Bari, 19 September 2026

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NF at scale: rare diseases with meaningful patient numbers

1 in 2,5k - 3k	1 in 25k - 40k	1 in 70k - 75k
NF1	NF2-SWN	Non-NF2-SWN

CTF estimates (managed population)



~4M worldwide

Why investors care

- Sufficient scale for multiple value-creating programs (not “one-and-done”).
- Validated biology and endpoints enable faster, more credible PoC than many rare diseases.
- Somatic NF1/NF2 alterations in oncology broaden strategic optionality beyond NF.

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The unmet medical need in NF1

Progress in plexiform neurofibromas leaves major needs across the lifespan

Clinical setting	The remaining treatment need
Cutaneous neurofibromas (cNF)	Reduce visible tumour burden, itch and discomfort with scalable, tolerable treatments
Low-grade / optic pathway glioma	Control progressive disease while preserving vision and neurological function
Wider NF1 burden	Further options for PN, malignant tumours, learning difficulties and daily functioning

Approved PN treatments are progress. NF1 needs a broader pipeline.

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Preclinical Hub
Network of Drug Selection Modalities

Platform – Basket Trials
Evaluating multiple assets in multiple manifestations

Clinical Trials Consortium

Drugs Scouting

Pharma

Educate & Improve Care

Research

Preclinical Infrastructure

Clinical Infrastructure

Liaise, Network, Consult

Approval

Community Education & Engagement
For diverse audience

Discovery Fund
Investment in new science & models

NF Data Portal

NF Clinic Network

NF Registry

Trial Endpoints

Regulators

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Carefully selected projects for the Preclinical Hub

Scientific advisors guide priorities, endpoints and translational relevance

NF1 project / resource	Purpose and current stage
Patient-derived and engineered iPSC resources	Mechanistic studies and drug screening Growing portfolio with further characterisation
Tumour models	Engineered PN models in development LGG/ OPG, MPNST xenograft resources forthcoming
Learning and behavioural models	NF1 mouse phenotyping ongoing Zebrafish models undergoing validation

The Hub connects suitable models, testing expertise and shared data

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Two promising candidates for clinical development

CTF actively searches for opportunities that address the remaining gaps

How we identified the opportunity	Proposed first application
Close collaboration with an industry partner	**cNF in adults**
Target and portfolio scanning	**LGG/OPG in children and young adults**

The next step is clinical evaluation through NF1-PEARL

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NF1-PEARL builds on the EU-PEARL framework

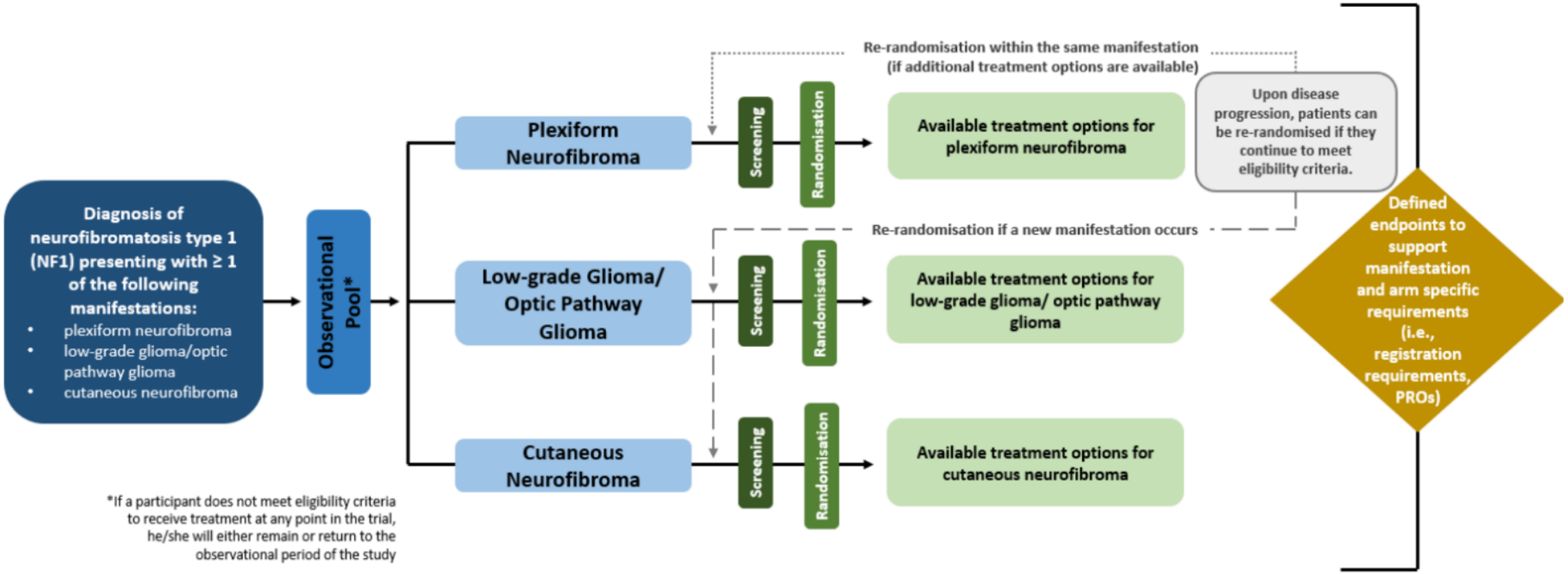
EU-PEARL
EU PATIENT-CENTRIC CLINICAL TRIAL PLATFORMS

An open-label Phase I/II platform with separate evidence for each intervention

Level	What it specifies
Master protocol	Common screening, observational follow-up, governance and core procedures
Manifestation	Population, clinical assessments and response definitions
Arm-specific appendix (ASA)	Dose, additional eligibility and safety requirements, sample size and decision rules

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Participation can continue across treatment arms



Treatment depends on eligibility and availability. Re-entry requires re-screening.

Two candidates, two clinical questions

Current implementation plan, September 2026

	cNF	LGG/OPG
Population	Adults with measurable, clinically burdensome cNF	Children and young adults with progressive / recurrent LGG/OPG
Stage	Single-arm Phase II	Phase Ib/II Safety and PK lead-in
Evidence focus	Tumour response, patient burden and durability	MRI response, visual function, safety and quality of life

Separate analyses and Go/No-Go decisions within one platform

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Patients helped shape the design

Teenagers with NF1 and families contributed through workshops in the UK, France and Spain

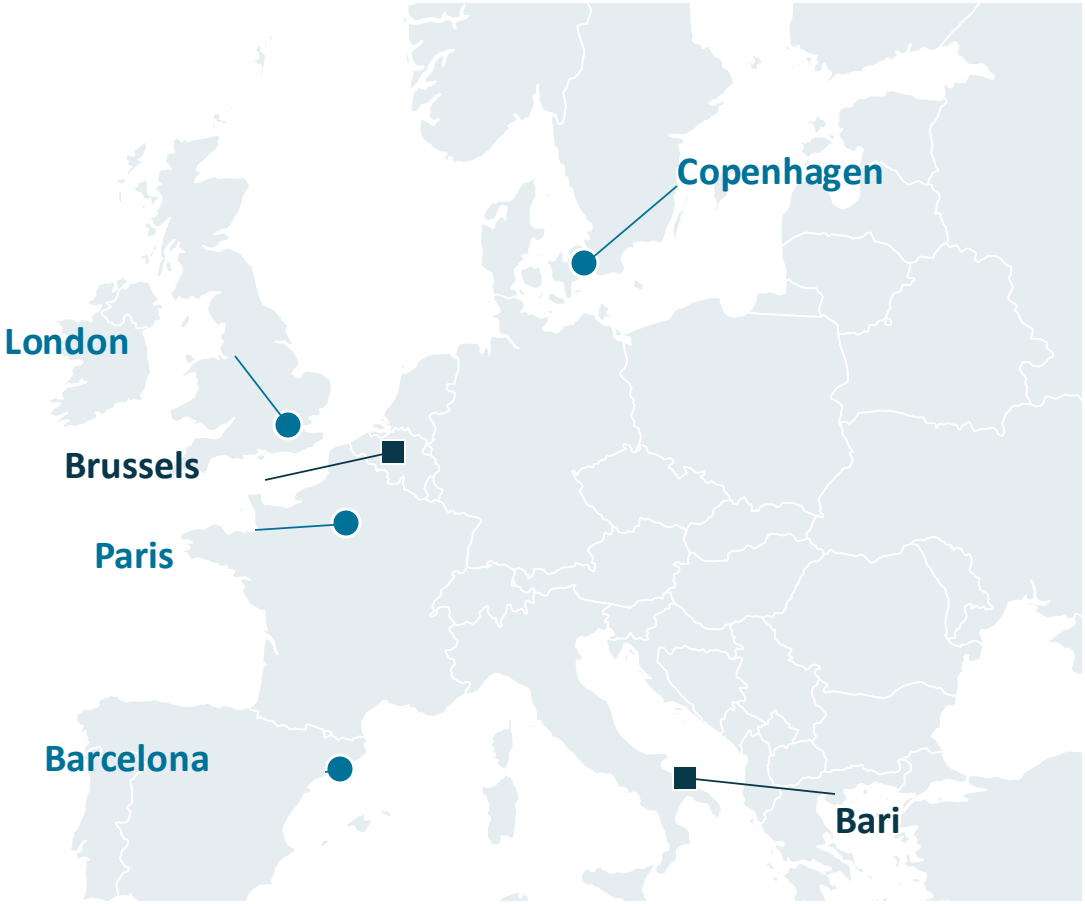
Meaningful benefit	Patient input helped add pain to the PN response assessment, alongside MRI
Manageable participation	The protocol reduced visits and aligned them with usual care where feasible

Continued patient involvement is part of the proposed trial's delivery

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NF1-PEARL's initial European footprint

Four clinical centres, supported by CTF Europe and CVBF

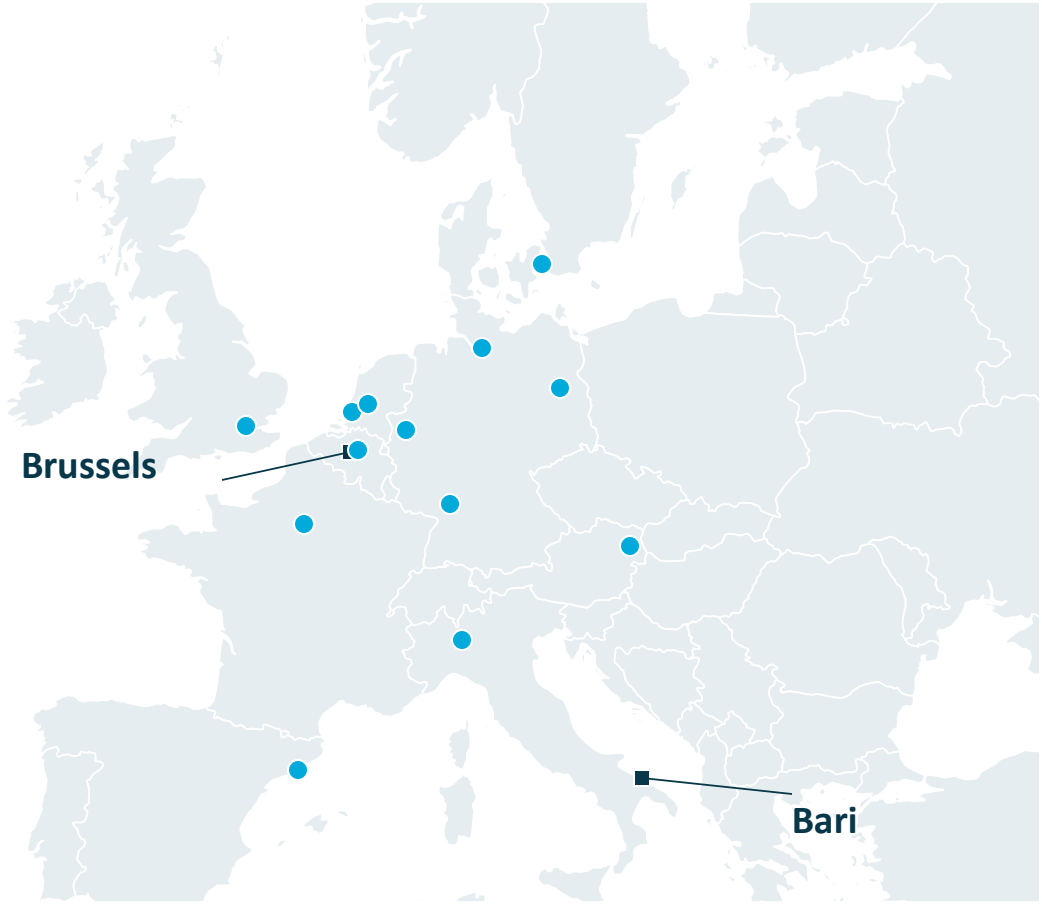


- NF1-PEARL core
- **CTF Europe / CVBF**

A focused opening network with room to grow

EU-PEARL's clinical site network

All sites listed in the NF network report



Multiple clinics may share a city marker

- **Clinical sites**
- CTF Europe / CVBF

EU-PEARL
EU PATIENT-CENTRIC CLINICAL TRIAL PLATFORMS

13 city locations

Across 9 European countries

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Paediatric oncology links for LGG/OPG

SIOPE-LGG offers a route to additional specialist centres



Multiple clinics may share a city marker

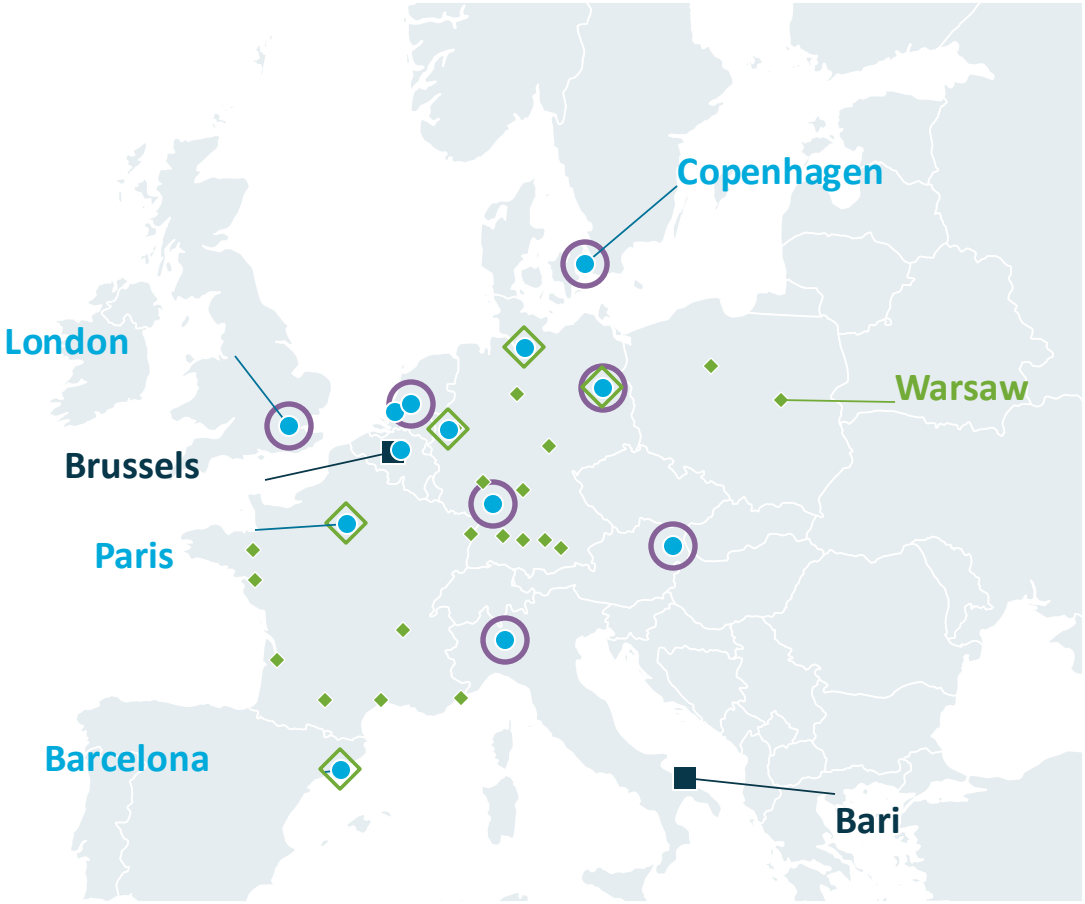
- EU-PEARL sites
- CTF Europe / CVBF
- **SIOPE-LGG sites**

SIOP Europe
the European Society for Paediatric Oncology

European paediatric oncology low-grade glioma group

NF Atlas adds a wider clinical community

Pilot mapping can inform future outreach and site feasibility



Multiple clinics may share a city marker

- EU-PEARL sites
- CTF Europe / CVBF
- SIOPE-LGG sites
- **NF Atlas centres**

> 30 NF Atlas pilot centres

Germany, France, Spain and Poland

The next milestones for NF1-PEARL

September 2026 implementation plan

Established	Work still required
Master protocol and completed EMA advice	Final arm appendices and arm-specific regulatory plans
ERDERA expression of interest submitted	Funding and final operational and supply agreements
Core centres identified in four countries	Recruitment feasibility, site preparation and trial approvals

60-month proposal within a 10-year master-protocol framework

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What other rare diseases can reuse

Reusable foundation	Work specific to the next disease
Master-protocol structure and templates	Natural history, eligible populations and treatment context
Patient involvement methods	Outcomes that matter and acceptable participation burden
Governance, data standards and quality processes	Measurement validity and a credible comparison strategy
Rules for adding or stopping arms	Intervention-specific safety and regulatory evidence needs

Reuse needs viable recruitment, valid outcomes and sustainable delivery

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Thank you!

Questions?

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How the platform evaluates activity

Within each arm

A predefined response endpoint

An arm-specific activity benchmark

Optional interim stopping for futility

Across the platform

Separate analyses by intervention and manifestation

No planned head-to-head efficacy comparison

Current master protocol: frequentist decision rules

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The regulatory boundary

EMA Scientific Advice on the master protocol, February 2025

Early development

The platform offers a reasonable way to select interventions for further investigation

Confirmatory evidence

A benchmark comparison alone cannot establish confirmatory efficacy

Each intervention and manifestation needs its own regulatory evidence plan

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Backup: response definitions in the master protocol

	cNF	LGG/OPG
Primary assessment	Month 12	Month 6
Tumour response	At least 5 of 10 target lesions show CR/PR, with no target-lesion PD during the period	CR/PR at Month 6, with no earlier PD during the first 6 months
Additional clinical context	Patient-reported burden, itch and durability	Visual acuity in OPG, function and quality of life

Final arm appendices must resolve estimands, missing data and follow-up

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