

THE FRENCH NATIONAL REGISTRY OF FSHD: A SPRAWLING HUB-AND-SPOKE ARCHITECTURE



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CONTEXT

Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common genetic muscular dystrophies in adults, affecting at least **3200 people in France**¹⁻³. The disease typically manifests as **asymmetric progressive muscular weakness**^{4,5}. The muscles first affected are those of the face, the shoulder girdle and the upper arm. The first symptoms usually appear in the late twenties. The severity and localization of the **symptoms are highly variable** among individuals even inside a single family. Although causal mechanisms are **complex and have not entirely been elucidated yet**, 95% patients feature a **shortened D4Z4 array on chromosome 4**, which constitutes type 1 FSHD. More complex etiologies are commonly referred to as type 2 FSHD. There is **no treatment**, but **experimental drugs are currently tested** in phase 2 and 3 international clinical trials. The French registry on FSHD⁶ has been started with the aim, in particular, to help **design and facilitate the setup of such trials**. The registry was created in 2013 and has been **funded and supported since then by AFM-Téléthon**.

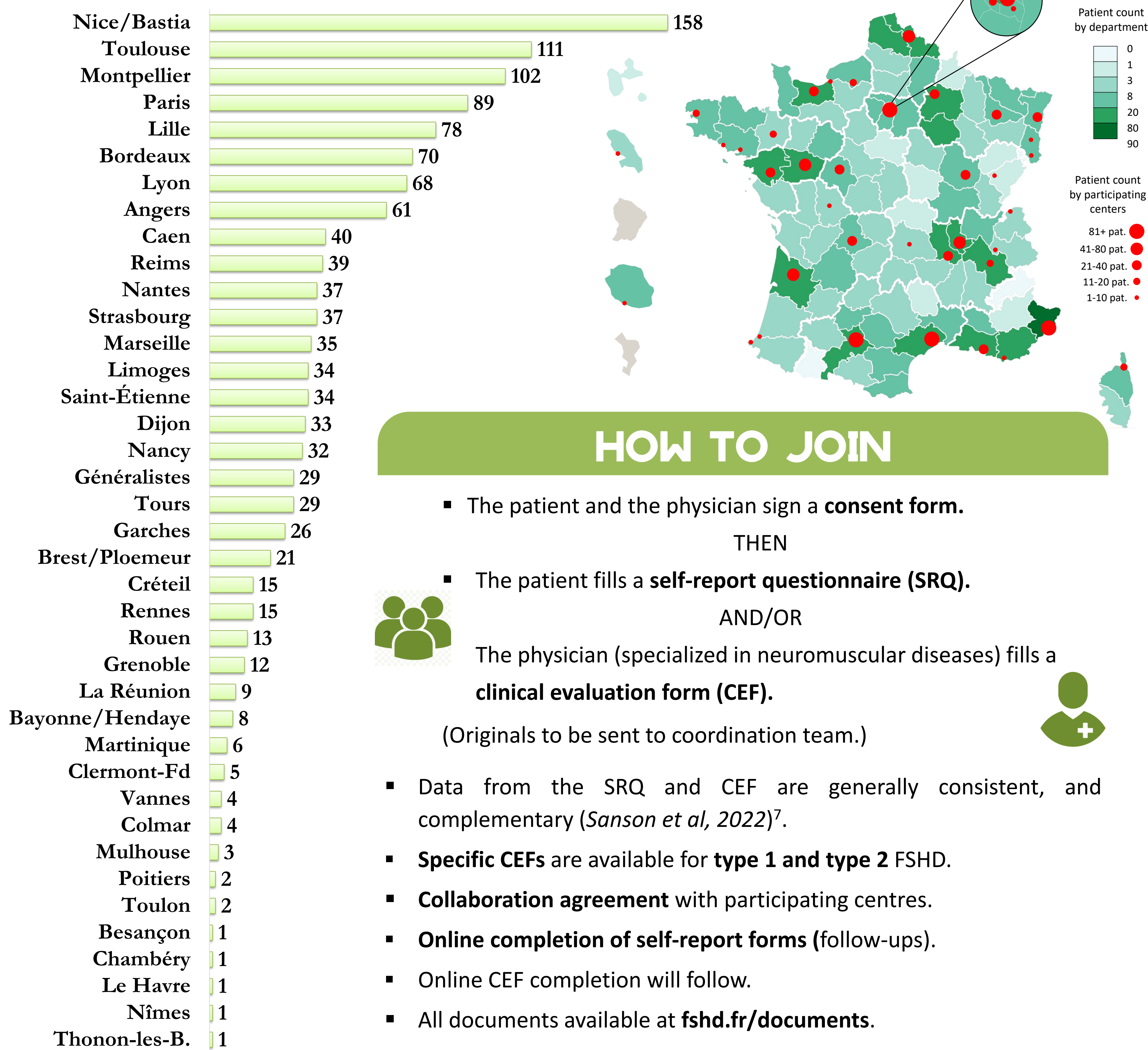
ORGANISATION & STRUCTURE

A COLLABORATIVE ENDEAVOUR

- Financed by AFM-Téléthon
- Coordination & clinical curation:** Prof. Sabrina SACCONI, Benoît SANSON & Sarah AIT BENAMARA (CHU Nice)
- Genetic curation:** Dr Rafaëlle BERNARD & Sitraka RABARIMERIARAJAONA (AP-HM)
- Bioinformatics:** Prof. Christophe BÉROUD (AMU) & Céline GUIEN (Genomnis)
- Valorisation, Regulatory & Statistical support:** Hadrien DELATTRE, Dieynaba DIAGNE, Juliette PETERKA, Caroline STALENS & Julie LEJEUNE (AFM-Téléthon)
- 41 participating centres** across France
- Steering committee**
- Networking with patient associations & consortia**
- A **database** and a **website**: fshd.fr



Distribution of patients in participating centres



HOW TO JOIN

- The patient and the physician sign a **consent form**.
- THEN
- The patient fills a **self-report questionnaire (SRQ)**.
- AND/OR
- The physician (specialized in neuromuscular diseases) fills a **clinical evaluation form (CEF)**.
(Originals to be sent to coordination team.)
- Data from the SRQ and CEF are generally consistent, and complementary (Sanson et al, 2022)⁷.
- Specific CEFs** are available for **type 1 and type 2 FSHD**.
- Collaboration agreement** with participating centres.
- Online completion of self-report forms** (follow-ups).
- Online CEF completion will follow.
- All documents available at fshd.fr/documents.

A TOOL FOR PATIENTS & RESEARCHERS

- Identification of potential patients in **therapeutic trials** : Fulcrum Therapeutics phase II ReDUX4 (NCT04003974) and phase III REACH (NCT05397470); CHU Nice phase II REINFORCE (NCT06222827).
- Switching to **nominative data** has made the **recruitment** of patients in trials **easier**.
- Information relay** towards resources on research and care, patient association and consortia websites.

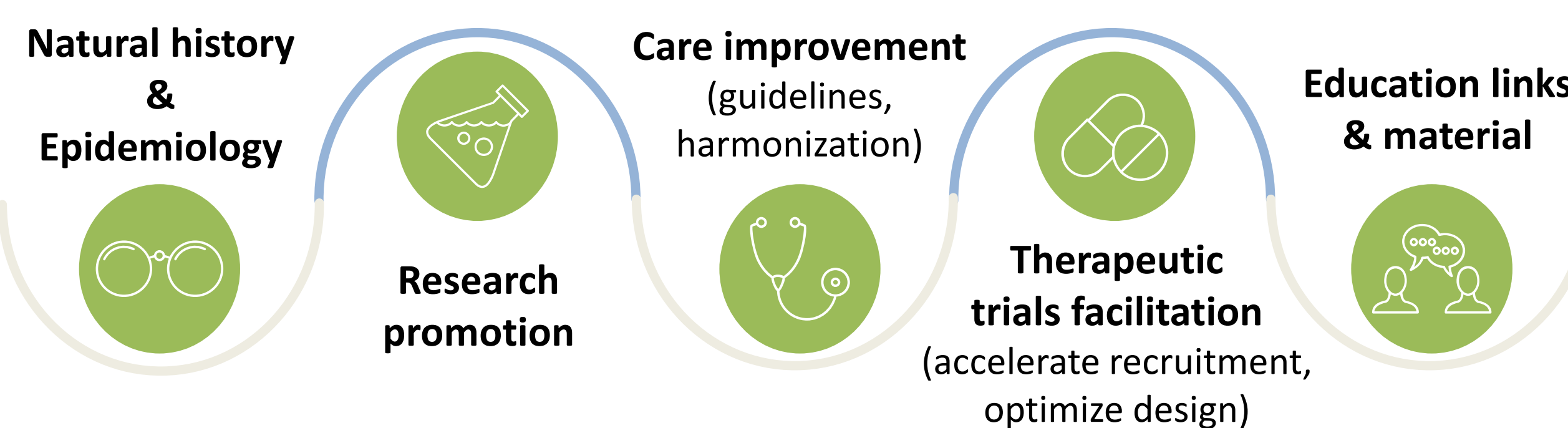
A HUB FOR RESEARCH PROJECTS

- Health Data Warehouse** status sought to allow more flexibility in the setup of future research projects.
- Clinical trial data** on the natural history of FSHD1 **integrated as registry modules**. *CTRN FSHD France* (NCT04038138) and *ADVANCED FSHD-COM* (NCT05453461) aim to optimize outcome measures beneficial in tailoring future clinical trials for ambulatory and non-ambulatory patients, respectively.
- Additional modules to be progressively set up** with studies complementary to *CTRN*, i.e. targeting, potentially, type 2 (*INSIGHT FSHD2*) and pediatric populations.
- Statistical analysis** on phenotypical and genotypical traits of **typical vs atypical** FSHD (article in preparation).
- Collaboration with a team in **CHU Tours** to better characterize **atypical features** (article in preparation).
- PhD doctorate financed to **apply machine learning** on the registry data.
- Setup of a **consortium with University of Kansas** to further **AI data analysis**.

References

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GOALS



DATA COLLECTION & QUALITY

- Inclusion & Follow-up data.**
- Nominative data** (phone numbers & email addresses) will allow to send :
 - Notifications facilitating the design and set up of future clinical trials;
 - Reminders to help collect longitudinal data.
- New set of forms** (June 2021):
 - Updated Forms;
 - Follow-up self-report;
 - Pediatric forms.
- Data monitoring** in centres being implemented.

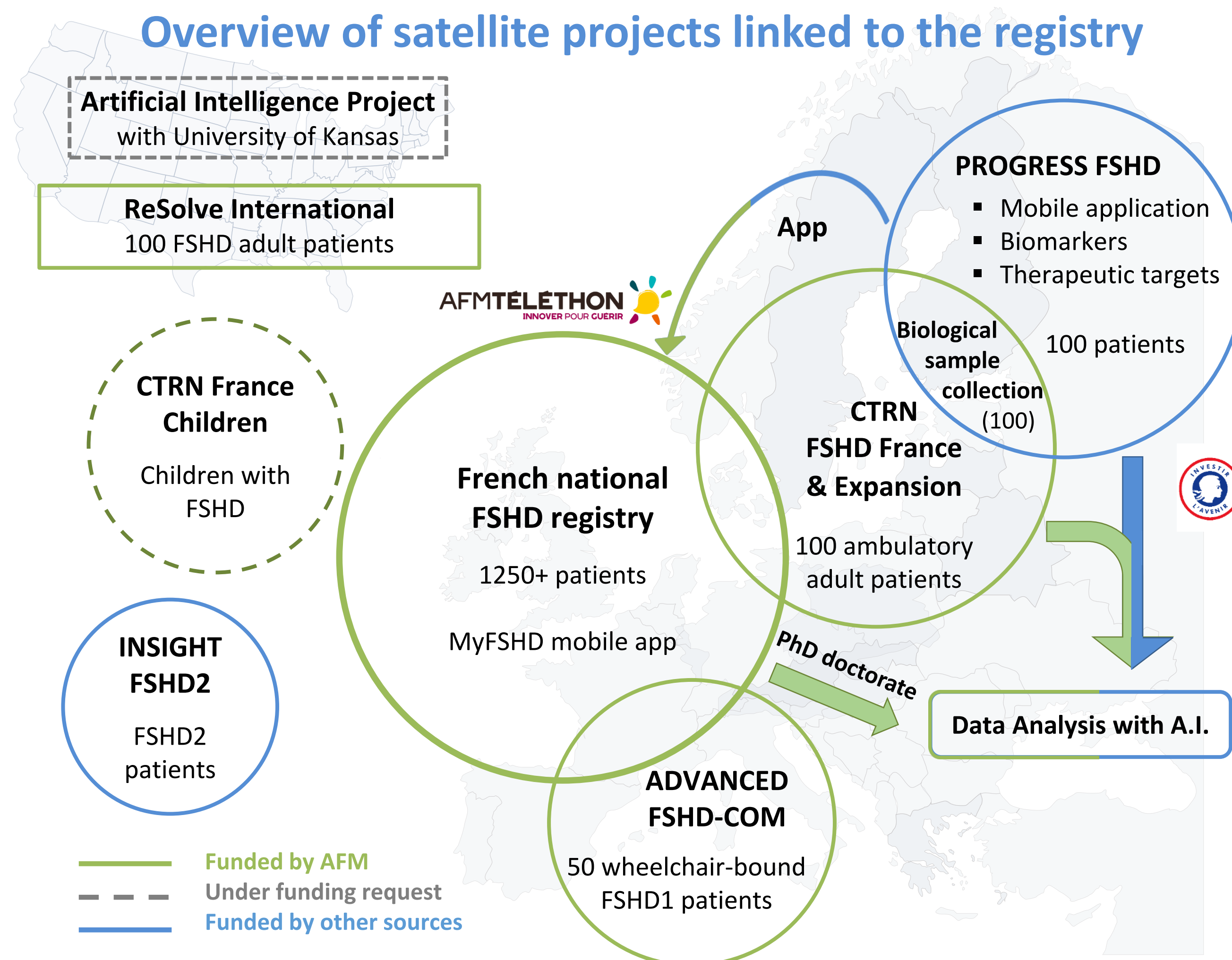
KEY NUMBERS

- 1266 patients**
- 3396 forms in total**
 - 1559 self-report forms
 - 1837 clinical evaluation forms
 - ~1300 follow-up forms (on March 1st, 2024)
- Data collection since 2013**
- New data protection authority (CNIL) authorization** in nov. 2020
- 2 scientific publications**^{6,7}
- 8 satellite projects** in progress or in development

DATA POLICY

- Valorization** through research projects and clinical trials : a dedicated committee has been set up to this end.
- Access to data is controlled and secured** ; login is made through a **2-factor authentication** process. **RGPD** requirements have been or are being implemented; data are hosted by a service provider that received the **French HDS certification for the hosting of personal health data**, since September 2019.
- Any use of data requires the **approval of the steering committee**.

Overview of satellite projects linked to the registry



FIVE-YEAR PERSPECTIVES

- Development of modules dedicated to **therapeutic education** available to patients who fill a form. Specific topics (e.g. nutrition) will be addressed.
- Real-World Data** collection (to identify clinical outcomes, help design clinical trials, etc.) through a smartphone app.
- Development a predictive model with **machine learning**.

Registry website : www.fshd.fr

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